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LEPTOTRICHOSIS CONJUNCTIVAE (PARINAUD'S CONJUNCTIVITIS) WITHOUT GLANDULAR INVOLVEMENT

REPORT OF A CASE

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The case here reported is noteworthy because of the fact that of the 56 cases of leptotrichosis conjunctivae observed by me it was the only one in which there was no glandular involvement, and because I have found no such case reported in the literature.

REPORT OF CASE

Roger B., aged 2 years and 4 months, was admitted to the outpatient department of the Massachusetts Eye and Ear Infirmary Aug. 28, 1939. The patient's father stated that the left eye had become a "little red" three or four weeks previously. Otherwise the patient had always been in excellent health. The family owned no cats; there were cats in the neighborhood, but, so far as was known, the child had not come in contact with one of them. The result of the intradermal tuberculin test (1:1,000) was negative.

On examination the upper bulbar conjunctiva of the left eye showed an intensely congested, moundlike elliptic area, about 8 by 18 mm., elevated about 3 mm. The lower margin of the mound was 1.5 mm. from the corneal limbus. Just beneath the surface there were eight conspicuous, almost white, irregular spots, each about 1 to 2 mm. in diameter. There was no ulceration. Elsewhere than in the vicinity of the mound the conjunctiva was almost free from congestion. There was slight if any abnormal secretion. The child exhibited no photophobia, keeping the eye wide open. Neither preauricular gland was palpable or tender to pressure. A few cervical glands—as might be expected in any child—were barely palpable, but no more so on one side of the neck than on the other.

On August 28, for biopsy and bacteriologic examination, two small pieces of tissue, each including one of the white spots, were excised by Dr. Merrill King.

On September 5 the lesion was definitely smaller, the spots were less conspicuous, and were becoming confluent. There was still no glandular involvement.

On September 26 the lesion had almost completely disappeared. All that remained to mark its site was an area of conjunctival hyperemia, considerably smaller than the original lesion. No traces of the white spots remained. The preauricular gland was still not palpable.

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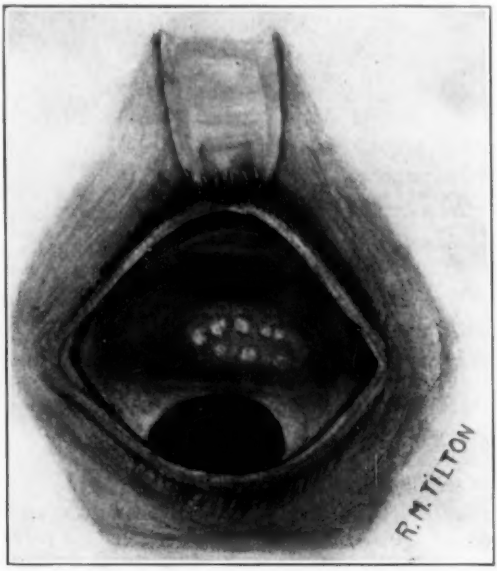
Read at the Seventy-Ninth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 4, 1940.

A clinical diagnosis of Parinaud's conjunctivitis was made, but owing to the absence of adenopathy the diagnosis was regarded as somewhat doubtful.

Bacteriologic Examination.—One piece of the excised tissue was ground up and emulsified in sterile physiologic solution of sodium chloride. The bacteriologic examination was then carried out, as described by King and me.[1] No growth of any kind was obtained on any of the mediums.

Histologic Examination.—The other piece of excised tissue was fixed in Zenker's fluid. Sections stained in hematoxylin and eosin showed typical lesions, such as I have previously described and depicted,[2] consisting essentially of foci of macrophages within a diffuse area of chronic inflammatory infiltration. Most of the macrophages were loaded with chromatin fragments resulting from cell necrosis. It was



Leptotrichosis of the bulbar conjunctiva without glandular involvement.

apparent that the white spots seen clinically did not represent single large foci but conglomerations of small foci. Eosinophils were not observed. No giant cells were present anywhere. Sections stained by Verhoeff's modified Gram stain[2c] showed typical leptotriches in large numbers within the foci of macrophages. In some sections they were as abundant as those depicted in figure 2 of a previous paper.[2c]

Final Diagnosis.—The final diagnosis was leptotrichosis of the bulbar conjunctiva, without adenopathy.

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1. Verhoeff, F. H., and King, M. J.: Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis): Artificial Cultivation of Leptotriches in Three or Four Cases, Arch. Ophth. **9**:701 (May) 1933.

2. (*a*) Verhoeff, F. H., and Derby, G.: Arch. Ophth. **33**:398, 1904. (*b*) Verhoeff, F. H.: ibid. **42**:345, 1913; (*c*) Am. J. Ophth. **1**:705, 1918.

Why glandular involvement failed to occur in this case can only be conjectured. That the lesion, although unusually large, was confined to the bulbar conjunctiva was probably an important factor. This, however, could not have been the only factor, since in all other cases of leptotrichosis observed by me in which the lesion was situated in the bulbar conjunctiva there was marked inflammatory enlargement of the preauricular gland. Another probable factor was the unusually rapid development of high resistance to the infection. This was indicated by the short duration of the infective process. It is my opinion that excision of part of the lesion for biopsy hastened the healing, possibly by permitting external drainage, but even with this consideration healing was remarkably rapid, especially in view of the size of the lesion. Of some possible significance in this connection was also the fact that this was the youngest patient that I ever encountered suffering from the disease.

The fact that the present case is the only one of leptotrichosis conjunctivae without glandular involvement thus far reported does not necessarily indicate that such cases are exceedingly rare, for this seems to be the only case in which an attempt was made to demonstrate leptotriches in a conjunctival lesion resembling those described by Parinaud but unassociated with glandular involvement. Moreover, few other investigators have demonstrated the presence of leptotriches in the lesions, even in suspected cases of Parinaud's conjunctivitis with adenopathy. This probably has been due not to the absence of these micro-organisms in many of the cases but to failure to employ a suitable technic or to find the essential lesions in which leptotriches are sufficiently abundant to be readily recognizable.

Certain observers, for example, Hamburger,[3] after investigating a few cases of oculoglandular tularemia and completely disregarding my observations, have drawn the unwarranted conclusion that Parinaud's conjunctivitis is due to tularemia. Many others, with equally limited experience in regard to the question under discussion, after investigating a few cases of conjunctival tuberculosis, have concluded that Parinaud's conjunctivitis is due to tuberculosis. All that this conflicting evidence indicates is that tularemia or tuberculosis may attack the conjunctiva and at the same time involve the preauricular gland, facts that were previously well established.

During the past thirty-five years, owing to the fact that my interest in the question of Parinaud's conjunctivitis was well known, I have had referred to me an exceptionally large number of patients believed

3. Hamburger, F. H.: Arch. f. Ophth. **137**:419, 1937.

to be affected with this disease. In fact, to judge by the literature, I have had an opportunity to study a much greater number of such cases than has any other single investigator. In 56 of these cases microscopic examination revealed the characteristic lesions which I have described, and in all but 2 cases the presence of leptotriches was demonstrated in the tissues. In these 2 cases the failure to isolate leptotriches was due to insufficient material. However, in 1 of these cases cultivation of the micro-organism was successful.

Parinaud,[4] in his 3 cases, did not investigate the histologic structure of the lesions, and the clinical features described by him did not suffice to establish a disease entity. However, the evidence he presented points more strongly to leptotrichosis than to tuberculosis or tularemia. Parinaud himself excluded tuberculosis as a factor in his cases, because of the absence of ulceration and the occurrence of prominent vegetations. As a matter of fact, these features do not exclude tuberculosis but do seem to exclude tularemia. It would seem best, therefore, either to abandon the term Parinaud's conjunctivitis entirely or to restrict its use to leptotrichosis conjunctivae. To abandon the term would be difficult, since it has been firmly intrenched in the literature for fifty years. In Boston, at least, the term Parinaud's conjunctivitis is a synonym for leptotrichosis conjunctivae.

The designation Parinaud's (oculoglandular) syndrome is now often employed, although, so far as I know, no attempt has been made to define it precisely. By modifying Parinaud's own conception, the term probably could be defined so as to include all cases of conjunctival leptotrichosis, tuberculosis or tularemia in which there is involvement of the regional lymph glands. So defined, it would be a convenient term to employ for certain purposes, for example, as a diagnostic designation before the exact nature of the condition in question was determined. It would, of course, exclude certain cases—for instance, the one here described—which rightfully belong in the same category.

The interest shown in Parinaud's conjunctivitis seems to be entirely out of proportion to the importance of the disease, for in no case has it been known to result in blindness or even in impairment of vision. It is, however, a spectacular condition, one that is alarming to the patient and one that may be the cause of prolonged discomfort. It is also a source of apprehension to the ophthalmologist, when, as is usually the case, he is unable to make a positive diagnosis and is, therefore, uncertain as to the prognosis. For these reasons early diagnosis is of importance in relieving the anxiety of both the patient and the ophthalmologist and in preventing the use of unnecessary treatment which might be

4. Parinaud, H.: Rec. d'opht. **11**:176, 1889.

unpleasant or even harmful. Moreover, the excision of tissue necessary for arriving at a positive diagnosis shortens the course of the disease.

The diagnosis of leptotrichosis conjunctivae can generally be made correctly from the clinical picture alone. The gray spots that I have described as occurring just beneath the surface of the lesions are especially characteristic. However, I have encountered a few cases of conjunctival tuberculosis which, on clinical evidence, I regarded as possibly cases of leptotrichosis, and vice versa. I have never observed a case of oculoglandular tularemia, but from the reports in the literature it is evident that ulceration is characteristic of this disease. Ulceration of the conjunctiva has not occurred in any of my cases of leptotrichosis. Fever and other systemic symptoms are always far less marked with leptotrichosis than with tularemia.

As has been indicated, judging by my own experience, the diagnosis of leptotrichosis can be made with certainty from the microscopic observations alone if the sections contain one or more characteristic foci of macrophages and no foci of epithelioid cells. Obviously, failure to find typical foci does not exclude leptotrichosis, since the excised tissue may not have included the essential lesion—the disease can be excluded only when lesions characteristic of some other disease—for instance, tuberculosis—are found. Originally, following Mallory's classification, I termed the phagocytic cells within the foci endothelial phagocytes, but I now prefer the term macrophages, which carries no implication as to the origin of these cells. These foci are, of course, the gray areas characteristic of the clinical picture.

In no case have I been able to demonstrate the presence of leptotriches in the tissues when no typical foci of macrophages could be found. To demonstrate these micro-organisms it is important that the tissues be fixed in Zenker's fluid. Sections from different levels should be stained slightly with hematoxylin and eosin, after which those sections showing the largest foci of macrophages should be stained by the modified Gram method. It is not necessary to decolorize these sections before thus restaining them.

Cultivation of the organisms from the conjunctival lesions is too difficult and uncertain often to be of value in arriving at a diagnosis. I have made no attempt at cultivation of tissue from the preauricular gland, fearing that this procedure might cause the gland to break down. Of the first 4 cases in which cultivation from the conjunctiva was attempted it was successful in 3,[1] but in a subsequent series of 7 cases success was attained only in 2. Leptotriches were demonstrated in sections in all except 1 of the successful cases; in the latter the failure to isolate the organism was explained by the minute size of the two foci of macrophages included in the sections.

SUMMARY AND CONCLUSIONS

A case of leptotrichosis conjunctivae without involvement of the preauricular or other regional lymph glands is reported. Microscopic examination showed lesions typical of this disease, and numerous leptotriches were demonstrated in sections.

Assuming, as seems most probable, that the conjunctival disease inadequately described by Parinaud is leptotrichosis conjunctivae, it can now be said that adenopathy is not an essential feature of Parinaud's conjunctivitis.

STRIAE RETINAE

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Anderson,[1] in his monograph on detachment of the retina, adopted the name of striae retinae for the white lines which may appear after reattachment.

According to Rönne,[2] these streaks are prominent ridges of connective tissue which develop between the retina and the pigmented epithelium. In 1918 Klainguti [3] came to an identical conclusion.

Van der Meer [4] in his thesis on detachment of the retina, devoted a few lines to a retinal condition which he supposed represented the anatomic substrate of striae retinae. In studying the anatomic structure of angioid streaks,[5] I encountered the specimen described by van der Meer, the condition it presented being ophthalmoscopically related to angioid streaks.

REPORT OF A CASE

In April 1919 a girl, L. N., consulted Dr. Hoefnagels. After an attack of influenza in December 1918, vision in the left eye, which had always been poor, became worse. On ordinary examination the anterior segment appeared to be normal, but on slit lamp examination a fine dustlike opaqueness could be detected. There were also fine dustlike opacities and some larger opacities in the vitreous body. The margins of the optic nerve were not quite sharp, but the vessels were normal. A detachment was found in the superior and nasal regions, which, however, did not extend far enough to reach the optic nerve. A rupture could not be traced. In November 1919 the dialysis had increased in size and could be seen bulging into the vitreous body like a low tension balloon but still not completely hiding the optic nerve. On May 20 the patient returned with absolute glaucoma. Miotics did not influence the tension, and on June 1, 1920 the eye was enucleated.

ANATOMIC APPEARANCE OF ENUCLEATED EYE

This eye has been extensively described in van der Meer's thesis. The retina is detached for the greater part, but in many regions the

1. Anderson, J. R.: Detachment of the Retina, New York, The Macmillan Company, 1931, p. 8.

2. Rönne, H.: Arch. f. Ophth. **75**:284, 1910.

3. Klainguti, R.: Ztschr. f. Augenh. **50**:71, 1923.

4. van der Meer, B. C. J.: Over de operatieve behandeling van netvliesloslating, Thesis, Maastricht, Netherlands, 1935, Maastricht, Stals, 1935.

5. Hagedoorn, A.: Angioid Streaks, Arch. Ophth. **21**:746 (May); 935 (June) 1939.

detachment appears to be a postmortem artefact. The rods and cones have either disappeared almost completely all over the retina or are difficult to trace; the nuclear layers are generally well preserved. A regular layer of pigmented epithelium is present almost everywhere.

Two regions are of special interest:

1. The first region shows the striae already traced by van der Meer. In the sections focal degeneration is seen in the inner part of the retina. The structure is demonstrated in figure 1. Evidently the lesion is the result of focal degeneration of retinal tissue together with proliferation of retinal elements (glia). There are no signs of inflammation (leukocytes and lymphocytes) or of mesodermal activity (fibroblasts). The

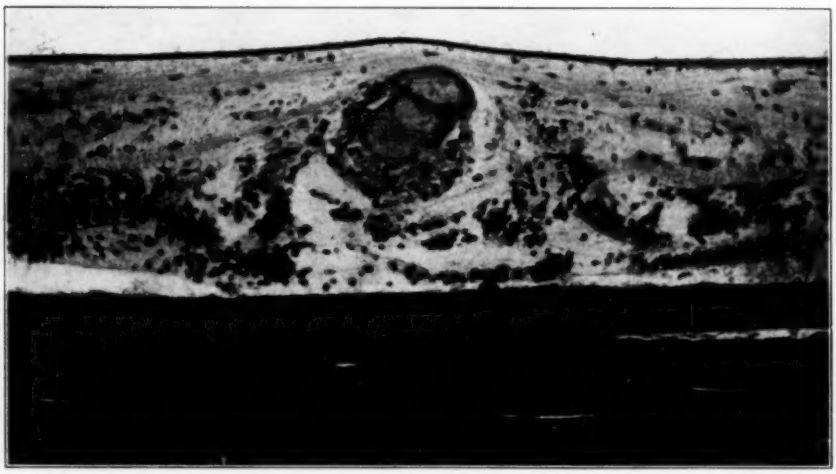

Fig. 1.—Section of the retina showing focal degeneration in the inner part of the retina. Van Gieson's stain; × 122.

lesion could be followed in all of the sections, and a reconstruction was made (fig. 2).

The circular area which appears darker at the top of the striae in figure 1 is due to the red color of the tissue, which is also seen in the mesodermal connective tissue. However, there are no fibroblasts, so that this material is a product either of retinal degeneration or of glial activity. A similar color may be seen in pathologic portions of the retina and the vitreous body in other regions of the specimen. There are no elastic fibers.

In a certain region the retina has a foldlike appearance (fig. 3). Here a connection of the striae with subretinal tissue becomes evident.

2. A smaller focus of degeneration in another region of the retina is also of interest, since here the disease is less severe but is certainly

identical with that previously described. This area of degeneration is continuous with a delicate, loose, fibrillar tissue between the retina and the pigmented epithelium. The tissue is identical with that previously

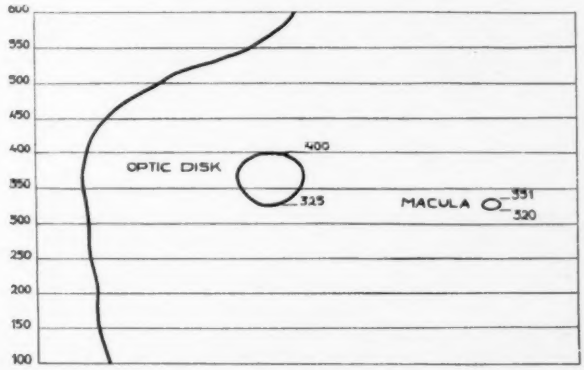

Fig. 2.—Reconstruction of striae retinae with optic disk and macula.

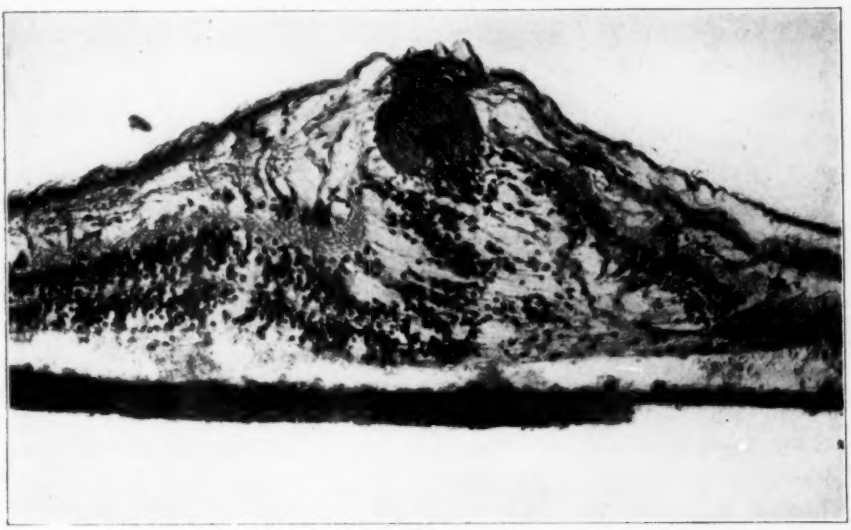

Fig. 3.—Section of the retina showing its foldlike appearance. Hematoxylin and eosin; × 130.

described in a case of traumatic rupture of the pigmented epithelium,[6] so that it probably originated from glia and pigmented epithelium.

The activity of the pigmented epithelium is demonstrated in the desquamation of pigmented cells, associated with a loss of pigment and

6. Hagedoorn, A.: Am. J. Ophth. **20**:13, 1937.

a change to spindle-shaped cells. Good photographs of this phenomenon could not be obtained, since the sections were made at a time when it was not possible to cut them thinner than 25 microns. Although many cells lost their pigment, several pigmented cells or heaps of pigment are present in the outer part of the striae. Since it has been borne out that hemorrhage may play a role in the development of striae, a test was made for the presence of blood. The results were negative. The inner, retinal, part of the striae was always free from pigment, which accounts for the white aspect of the striae in the fundus.

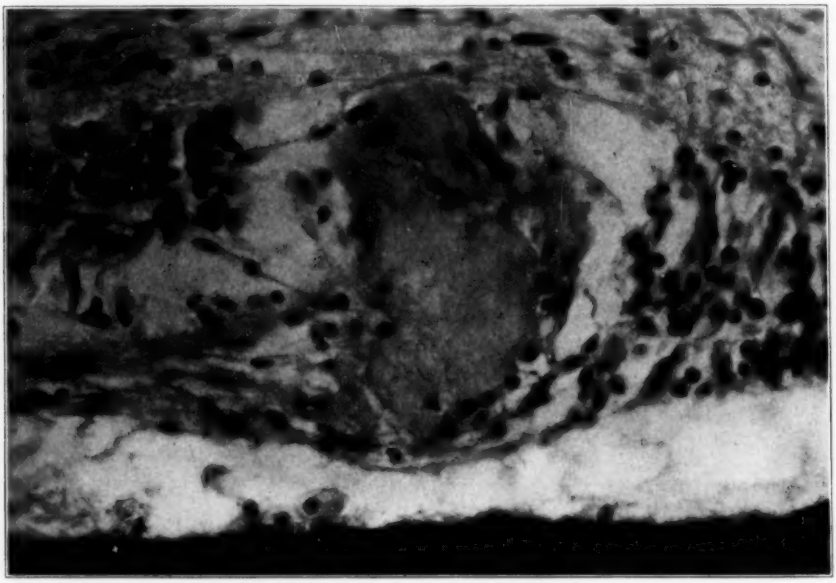

Fig. 4.—Periphery of the retina. Hematoxylin and eosin; × 385.

In many other regions the pathologic condition, especially of the outer layer of the retina (rods and cones) and perhaps of the pigmented epithelium, was the stimulus for the development of a similar fibrillar tissue between the retina and the pigmented epithelium.

Since there can be no doubt that Rönne and Klainguti have described true cases of striae retinae, it has to be concluded that in later stages the newly formed tissue will become more solid and dense, acquiring the features of connective tissue. This may occur by a gradual transformation of loose glial tissue into fibrillar tissue, which is in accordance with Rintelen's findings [7] in disciform degeneration and with my conclusions regarding angioid streaks. Such a point of view fits in with

7. Rintelen, F.: Klin. Monatsbl. f. Augenh. **97**:673, 1936.

Masson's conclusions regarding tumors of nerve tissue.[8] It is also possible that in later stages fibroblasts secondarily may invade the described tissue and rebuild it into the connective tissue described by Rönne and Klainguti. A final decision will never be possible from a study of the sections, since fibroblasts are mobile cells.

Evidently the striae are a result of focal degeneration and glial activity in the retina. The peculiar linelike arrangement of the retinal process may be due to the continuous folding and bending of the retina along this line in the period of detachment. This prolonged trauma may cause a line-shaped degeneration of the retina, stimulating the activity of glial tissue. Since in these early stages degeneration is a most outstanding feature of the pathologic process, the possibility of a primary streak or linelike active growth of the glia comparable with that of the mesoderm in cases of retinitis proliferans has to be rejected. The fold-like appearance of the retina in figure 2 may be explained by this theory, though postmortem shrinkage may have played a part.

COMMENT

A similar process may be expected to occur at the borderline of normal and detached retina, resulting in the broad, pigmented, demarcation streak seen in localized retinal detachment of longer standing. Here both pigmented epithelium and retina are damaged and stimulated to proliferation by the prolonged trauma. This may also occur at the borderline of normal and detached areas in cases of detachment of the choroid (Bonnet[9]).

These pigmented streaks are essentially different from angioid streaks, which are ruptures in a degenerated Bruch's membrane, and from Siegrist's pigmented streaks,[10] which are due to proliferation of the pigmented epithelium following arteriosclerosis with associated pathologic cellular proliferation in the choroid.

CONCLUSION

The anatomic substrate of white retinal striae occurring after detachment is described. The striae are a result of a primary streaklike degeneration and proliferation of retinal tissue.

8. Masson, P.: Am. J. Path. **8**:367, 1932.
9. Bonnet, P.: Arch. d'opht. **3**:1, 1939.
10. Siegrist, A.: Cong. internat. d'opht. d'Utrecht (1899), 1900, p. 131.

A MICROSCOPIC STUDY OF THE CENTRAL LENS CAPSULE IN GLAUCOMA CAPSULARE

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One of the striking discoveries made with the slit lamp is the syndrome "exfoliatio capsulae anterioris lentis." Though it has been known for only two decades, the subject can boast of a history. Even the name under which it has been described has often been changed, coincident with the progress of knowledge.

In December 1939 and January 1940 two papers appeared in the English language, the first,[1] awarded the Middlemore prize for 1939, on the underlying causes of glaucoma. Regarding the subject under discussion, Evans stated:

> Exfoliation of the anterior lens capsule has received attention from Vogt (1925) and in 1932 Sobhy Bey drew attention to its association with glaucoma, as also did Horven in 1937. These flakes are rubbed from the surface of the lens capsule by movements of the iris and then pass to the filtration angle which they appear to obstruct. Mallin, however, states that these flakes do not, in fact, block the filtration angle. This process of scruffing of the periphery of the anterior lens capsule is considered by Scandinavian authorities to indicate an underlying chronic uveitis which they consider to be the cause of glaucoma. These changes may provide additional factors favouring the onset or maintenance of glaucoma in predisposed eyes but cannot be considered as the causes of glaucoma *per se*. . . . In respect of exfoliation of the lens capsule, this process, in its origin, is determined by degeneration of the capsule, a process which is very probably due to an excess of toxic metabolites in the aqueous and to their prolonged retention on account of venous and capillary stasis in the canal of Schlemm system and the ciliary region.

A paper was presented by Irvine[2] before the Section of Ophthalmology of the American Medical Association at the meeting in St. Louis. In case 13 a few faint scratches were visible on the lens capsule but no exfoliation. In case 14, after dilatation, no definite exfoliation as characterized by frost or stippling of the lens capsule was seen; instead there were noted fine radial scratches vaguely suggesting exfoliation. Some fine pigment granules were seen interspersed between these

1. Evans, P. J.: Brit. J. Ophth. **23**:745, 1939.
2. Irvine, R.: A Study of Exfoliation of the Lens Capsule (Glaucoma Capsularis): Forty Cases of Exfoliation, Arch. Ophth. **23**:138 (Jan.) 1940.

scratches. Cases 13 and 14 are those to which reference was made in the text suggesting that scratches of the lens capsule may be the first visible signs of a change in the superficial layer preceding exfoliation. The description of case 25 is not very clear:

> The pupil dilated, revealing marked stippling and exfoliation on the capsule in sheets. The pupillary disk . . . formed a bridge continuous with the peripheral zone of the exfoliating capsule. This bridge . . . showed extremely fine radial stippling which stopped at the margin of the pupillary disk, merging into the relatively normal-appearing capsule of the disk. The capsule of the pupillary disk appeared definitely different from that of the periphery, both where the peripheral capsule was obviously exfoliating and where it presented a homogeneous gray appearance. . . . One got the impression that all the capsule in contact with the iris had been affected while the pupillary disk remained more normal.

In a historical review one must look for the first mention of this heretofore unknown condition. In Vogt's Atlas [3] (1921) are his findings of a ring on the central part of the anterior portion, partly in contact with a similar peripheral change, free from this iris. His interpretation was revoked in an instructive paper in 1925. In 1923 he published the first picture of "Flaumigue weisse Pupillarsaumauflagerungen nach Trepanation" (fluffy white deposits on the pupillary border with a disklike homogeneous pseudomembranous appearance). This was at least three years before its "first" picture appeared in "Contributions to Ophthalmic Science Dedicated to Dr. Edward Jackson." Vogt was under the impression that this disk may have been the result of the glaucoma. He thought the grayish white (*grauweisse*) turbid disk to be a very fine exudative deposit. He noticed total absence of any form of pigment and in 1923 stated: "Perhaps both formations, the turbid disk and the deposits of the pupillar zone, are products of one and the same substance."

In 1925 Vogt [4] published an article with a set of pictures. What little has been added to this text has been done by Vogt himself. The pictures have not been surpassed. The three pictures in the "Traité d'ophtalmologie" (vol. 6, 1939) with the half-page description of "glaucome capsulo-lenticulaire" are all taken from this paper of Vogt's. The first change observed is a soft grayish opacity and stippling of the capsular surface. One can postulate that the first signs are cracks, the result of an undermining of the lamellae by aqueous humor. Cracks must undoubtedly favor exfoliation. Pupillary fluff is therefore secondary. In his seventh case there was a triangular clump of this bluish white fluffy substance adherent to the posterior part of the cornea.

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3. Vogt, A.: Lehrbuch und Atlas der Spaltlampenmikroskopie des lebenden Auges, Berlin, Julius Springer, 1921, fig. 142.

4. Vogt, A.: Klin. Monatsbl. f. Augenh. **75**:1, 1925.

Vogt later dismissed the theory of the formation by an exudate and accepted that of a change in the anterior lamella of the lens capsule. In his studies of the structure of the lens capsule during 1912 and 1913, he macerated the lens capsule and showed that it is formed of parallel lamellae, of which the oldest are anterior and the thickest. Heinrich Müller, in 1856, who himself referred back to Lomeyer and Broca, had found this same lamellar structure and had stated: "Sie (die Kapsel) wird nicht selten in Lamellen und Streifen spaltbar" (it [the capsule] frequently becomes cleavable into lamellae and bands). E. Berger published his observations on the lens capsule in 1882. He macerated the lens capsule in a solution of potassium permanganate and teased fragments. He referred to older investigators, who had come to diametrically opposite opinions. He found, as Mensonides did in 1848, a "streifige Beschaffenheit" (striated condition), which speaks for a lamellar structure. He mentioned Müller with these words, "A line would be seen on a fold, where the height of the capsule was 0.204 mm. for a certain distance, not just in the middle of the thickness, emphasized by granules and small particles." Vogt published a thorough study about the genesis of cataract in 1913. Maceration experiments showed a distinct lamellar structure of the lens capsule. One sees about ten to twelve parallel lines in a transverse section; they are shorter toward the epithelial side, which points to an origin of the capsule from the epithelium.[5] His pupil, Wiederkehr, mentioned that separation in individual lamellae was not successful.

Vogt described the light blue fluff, unpigmented, on the pigmented border of the iris, rarer on the adjacent stroma, or circummarginal. This material is an extraneous deposit and does not need to cover the entire iris ring. After the pupil is dilated the typical change of the anterior capsule may be seen. The pupillary region does not show the stippled pattern. The zone between the two regions is generally free, although occasionally remnants (the "bridges") cover it. Vogt published a picture (Abb. 9) in which no cracked line of the pupillary disk is seen. The disk is seen only because it is more grayish. The transition from opaqueness to a more transparent surrounding proves that the pellicle is not a foreign precipitation but part of the capsule itself. In 1926[6] Vogt related that in one place he found a second exfoliation in progress. Therefore, exfoliation of more than one lamella can take place, a proof that all of the superficial capsular layers may take part in the process. He found glaucoma in 80 per cent of his patients and considered glaucoma the result of obstruction by this same material.

5. Vogt, A.: Arch. f. Ophth. **88**:320, 1914.
6. Vogt, A.: Schweiz. med. Wchnschr. **56**:341, 413 and 426, 1926.

In 1928 Vogt [7] published the first histologic pictures of the condition, which are brought more and more to the attention of the slit lamp adepts. These illustrations removed all doubts and established the term glaucoma capsulare or capsulocuticulare (1928).

The rubbing off of the external capsular lamellae became the important process in the syndrome. It was called "exfoliatio cap-

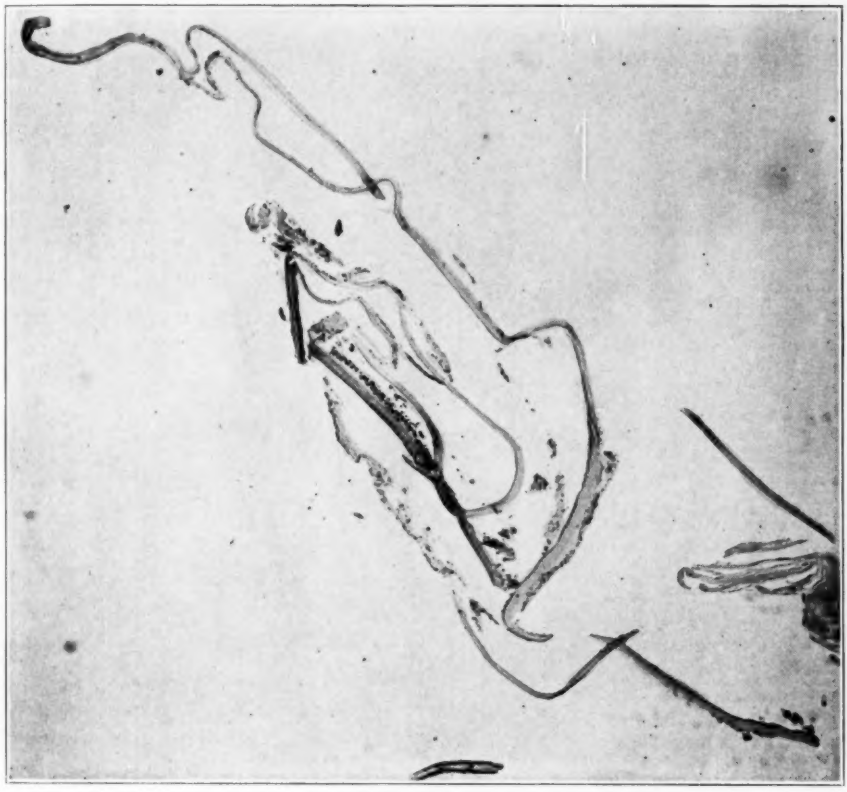

Fig. 1.—The capsular material under low magnification.

sulae anterioris lentis." These three expressions are indiscriminately used.

Vogt noticed in the capsule the presence of vacuoles, chiefly in the superficial, or older, part. It seems that these usher in the exfoliation. He found in a later case of typical glaucoma capsulare that the vacuoles were found also in the deeper layers, with a tendency to split the capsule in larger thicker lamellae.

7. Vogt, A.: Klin. Monatsbl. f. Augenh. **81**:711, 1928.

Vogt made these demonstrative observations on enucleated eyes, which I have been unable to duplicate, and he pointed out the incompleteness of the examination of pieces of capsule removed with the capsule forceps during extracapsular extraction of the lens. Still he gave the

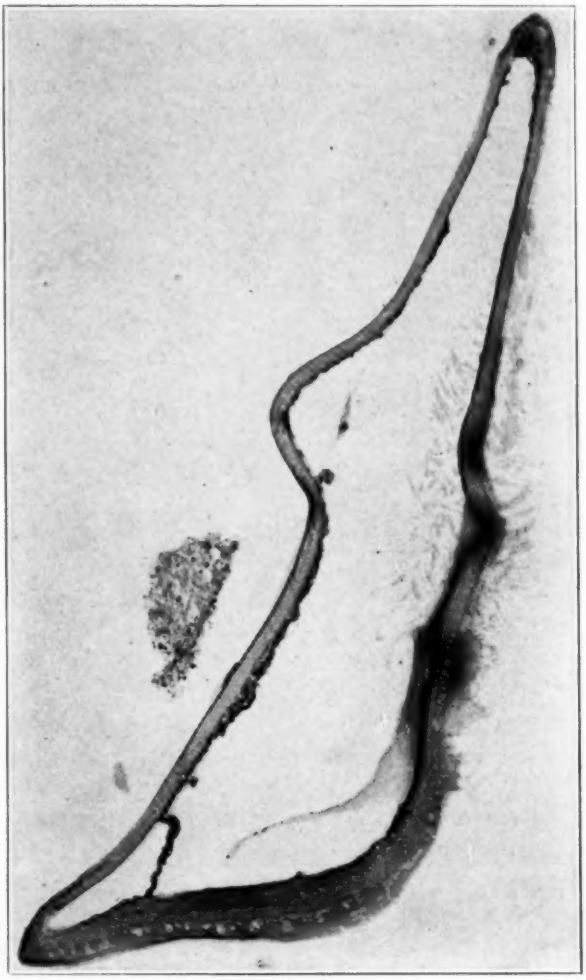

Fig. 2.—A horizontal section, with medium magnification, showing the vacuolation of all the strata of the capsule and the exfoliation at the outer side.

picture of such a piece and of pieces of lens capsule in 2 glassblower's cataracts with lamellar separation. It seems that this warning, which has been repeated in Wiederkehr's study (1938), has had its results in that I have been unable to find any report of the histologic examination of the capsule removed.

In the fall of 1939 I removed the capsule of a cataractous lens in a woman aged 65 years, who showed in both eyes the picture of exfoliation, diagnosed before slit lamp examination. With the help of Prof. Dr. K. Terplan, I can show a few slides, which I hope may be of interest.

The first illustration gives a general impression of the material. It shows at once the difficulty which confronts one.

Fig. 3.—A layer of pigment in the middle of the capsule, dividing the capsule, which shows exfoliation, in nearly two equal parts.

Figure 2 is a horizontal section, with medium enlargement, which shows well the vacuolation of all the strata of the capsule and the exfoliation at the outer side. The pigmentation of the inner side of the capsule seems important.

Figure 3 shows a layer of pigment in the middle of the capsule, dividing the capsule, which shows exfoliation, in nearly two equal parts. The layer is not formed by two separate parts of the capsule which accidentally came together, as seen in figure 4, which is the continuation of figure 3.

Figure 5 shows the entire capsule undermined by vacuoles, the smaller ones in the youngest parts, the bigger ones outside. These vacuoles are under pressure; when they escape from their neighbors they enlarge and take a balloon shape. Is it the cement substance or the lamellar tissue which resists bursting? Scattered throughout, but especially in the inner parts, granules of pigment are seen.

Fig. 4.—Continuation of figure 3.

Figure 6 represents a part of tissue which must belong to the subcapsular region because of its nuclei. The smaller dots are pigment outside direct influence of the iris. This is an enlargement of the outlying island of figure 2.

Figure 7 is an enlarged part of figure 1. It shows the pathologic splitting of the capsule. Here is a most instructive example of the formation of the normal capsule among pathologic changes. It is found in three separate slides.

As is to be expected, the sections of part of the central portion in 1 case of clinically proved glaucoma capsulare are of value only when due recognition is given to the many sections of the entire eyes given by Vogt. Still there is some satisfaction in seeing that those few sections demonstrate the essential features of Vogt's findings. The vacuolation, which is mentioned in some of Vogt's descriptions, is seen here and is

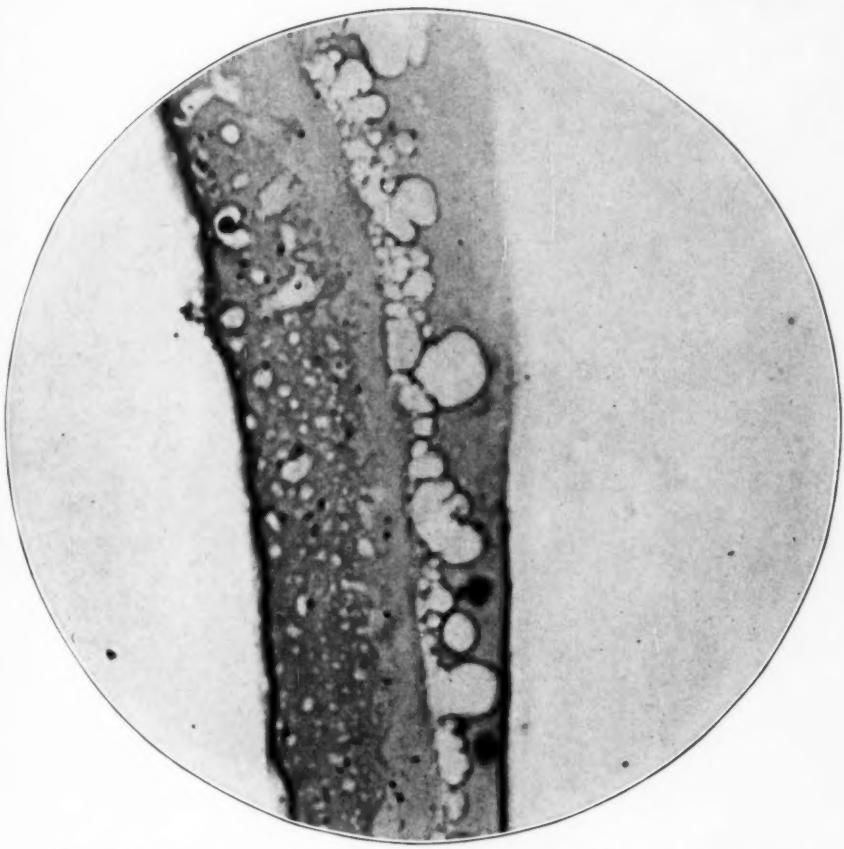

Fig. 5.—The entire capsule, undermined by vacuoles, the smaller ones in the youngest parts, the larger ones outside.

not limited to the external part of the capsule. Vogt in 1932 for the first time described as a new histologic picture his "Dissociatio Capsulae Profunda" (*Tiefenzerklüftung*). The age of the patient of this thesis is about twenty-five years below that of Vogt's patient.

The genesis of the vacuolation is still unexplained. It is not known if the "cement substance" is primarily or only secondarily affected.

There must be a difference in resistance toward whatever initiates the process. Is it really a local change in the lens or is the entire eye affected? Clinical signs of absence of cyclitis and infection must not be given a too prominent value; cytopathology is yet in its infancy. Figure 7 is in favor of the supposition that the cement substance is changed before the lamellar substance proper.

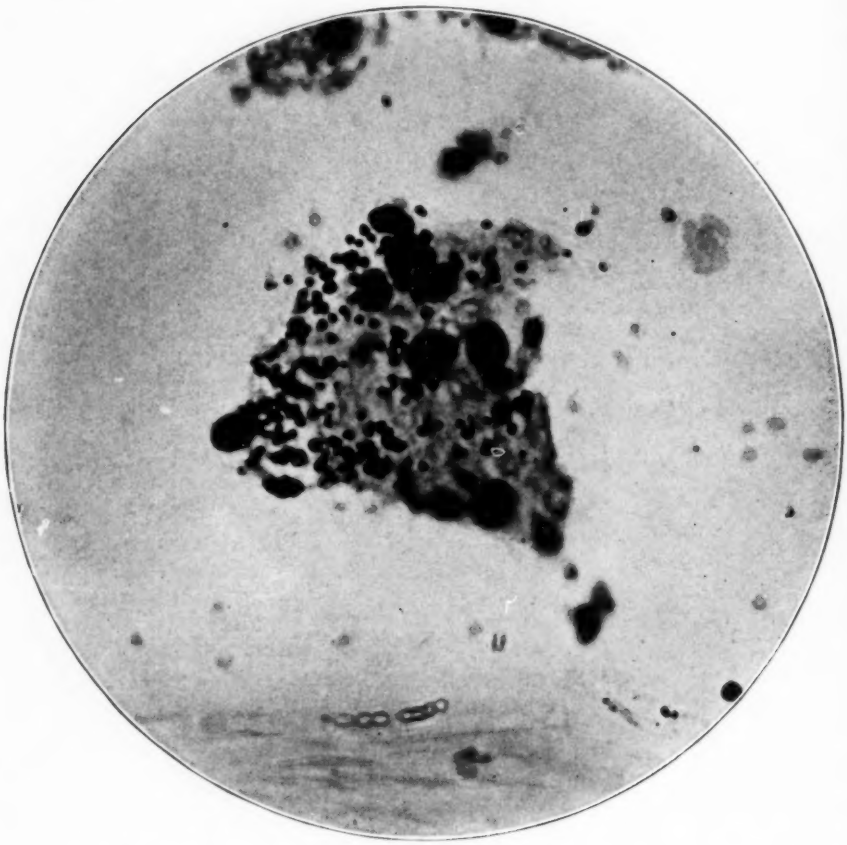

Fig. 6.—Enlargement of the outlying island of figure 2, showing some tissue which must belong to the subcapsular region because of its nuclei. The large dots are nuclei and the small ones granules of pigment.

Occasionally one finds in Vogt's reports (and also in Wiederkehr's) a description of some deposits of pigment but never in the way I have found it, within and under the capsule. That these pigmented granules (melanin) are below the capsule, not above it, is demonstrated by the intermingling with nuclei (fig. 5). They are found so frequently that the traumatic influence of the forceps can be excluded. These nuclei

can belong only to the capsular epithelium. The derivation of the pigment is difficult to explain. If a direct transport from the iris, or corpus ciliare, can be excluded (the sections under consideration do not give any indication of it), one may perhaps find that the origin is in the capsular epithelium. It is of epidermic origin. This sort of epithelium has the property to produce melanin, under appropriate

Fig. 7.—Enlargement of part of figure 1, showing the pathologic splitting of the capsule.

conditions, from its cellular protoplasm. Melanogenesis is an endocellular function, the production of condensation in the protein molecules (with absorption of oxygen and loss of water), of what is called the chromogenous group formed by the amino acids, tyrosine, phenylalanine and tryptophan. Bruno Bloch produced intracellular formation with dopa, proving the existence of a specific ferment—dopase—in the cells of the epidermis (M. H. Moutinho).

The melanin then found is of endogenous origin, the expression of an altered action of the epithelial cells of the lens capsule, these being of ectodermic origin.

The change in color of the "central disk" would then depend not only on the change in the capsule (increased thickness and vacuolation) but also on the formation of pigment.

Fig. 8.—This illustration gives another idea of how the capsule can split, or are the fine lines near the point of the section (inner side) remnants of the adhesions of the fibers of the zonula zinnii.

The capsular epithelium plays a prominent role in the selection of the substances which by osmosis from the aqueous humor can pass through the capsule into the lens. Recently Ashikaga used vital staining. He found between these cells "des corpuscules massues," which he considered to be safety valves for entrance or outlet of substances of the aqueous humor. Perhaps the first anatomic change of glaucoma

capsulare may be found in the capsular epithelium. Or could it be that a fluid like the one of the fluid clefts which is foreign to the lens substance, as is shown by the diffuse internal reflex of the walls of these slits being increased, leads to cloudiness, permeates the capsule epithelium, changes these cells' vitality and produces the degeneration of the capsule?

COMMENT

The foregoing study has raised many questions; for instance, is the lens capsule the product of the cells within the closed lens vesicle, or must the theory of the formation of the lens capsule at the time of the first thickening of the ectoderm, which initiates the formation of the lens, be accepted? Glaucoma capsulare does not show changes in the posterior part of the lens capsule. Vogt suggested a different origin of both parts, the anterior part a product of the epithelium cells and the posterior a condensation of fiber substance, while Dejean suggested as the origin a condensation of the lens and vitreous body limiting membranes.

Do the fibers of the ligamentum suspensorium adhere to the capsule in a narrow zone with the equator lentis as midline? Or do these fibers form a continuous sheet or bag around the whole lens? The investigations of Vogt seem more in favor of the first proposition. If so, the term "zonular lamella" could be limited to that part of the lens capsule where the fibers of the zonula zinnii adhere to the lens capsule.

It seems that a continuous membrane or lamella, formed by the zonular fibers or below these (Busacca) is not proved.

The anterior capsule consists of lamellae which are so firmly cemented together that one can speak of "une membrane anhyste;" they are formed by the layer of epithelial cells. The lamellae become separated only under pathologic conditions.

NOTE.—It seems that the primary seat of glaucoma capsulare is limited to the region of the capsule and its epithelium. This region is one of the four *grenzzonen* (marginal zones), the significance of which has been especially called to our attention by Walther Reichling and his co-workers. The other three regions are Bowman's membrane with its (corneal) epithelium, Descemet's membrane with its endothelium and the lamina vitrea with the retinal pigment layer. It has long been known to occur in the blood vessels.

The process of histolysis (Rössle) makes visible tissues which under normal circumstances are invisible. The matrix takes up fluid and enlarges. This fluid shows albuminous content of different amounts. Vacuoles appear apparently through precipitation of the liquefied matrix. A fibrillar spongelike material is produced. Sudan staining shows fat as a sign of this activity. Nuclei appear in this material, and vessels are attracted from the surrounding tissue, as, for instance, in the region of

the lamina vitrea and the retinal pigmented epithelium. Future examination in cases of capsular glaucoma should be directed toward finding out if this process of histolysis has taken place. It cannot be concluded that histolysis is the cause unless painstaking investigation of the entire eyeball is made. Most probably the process will be considered a degenerative one due to senescence, beginning with dystrophy of the capsular epithelium.

Tess found in a specimen of copper cataract a colored strip between the capsule and its epithelium and spoke of a fluid in a virtual space; this may perhaps have been the stained matrix of this *Grenzzone*.

VITREOUS, ZONULE AND CILIARY PROCESSES FROM A SURGICAL POINT OF VIEW

ESPECIALLY WITH REGARD TO OPERATIONS FOR CATARACT AND DETACHMENT OF THE RETINA

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A great many surgeons look on the vitreous as merely an inert mass of jelly having the structure and consistency of fresh white of egg. Moreover, they imagine that if one plunges a knife into the vitreous and then withdraws it, or if the hyaloid membrane ruptures, and a few drops of vitreous happens to escape, and the wound is then closed, no harm has been done. Nothing could be farther from the truth. In the first place it is more important to bear in mind that neither the eye nor the vitreous is a dead structure which can be operated on as one would do at autopsy, but that the eye as a whole, as well as all of its structures, is a living organ of dynamic soul-energy, having both physical and mental properties which react to every action on the part of the surgeon and influence the energy of the body, and especially the organ being operated on. There is abundant evidence to prove that everything which possesses life has at least a trace of subconsciousness, even the ameba, the blood corpuscles and all the lowest forms of life. This subconsciousness develops into instinct in many of the invertebrates, especially insects, such as ants, bees and wasps. In higher animals, especially birds and mammals, it shows further development and exhibits definite intelligence, as every one can see. Wallace [1] definitely and unmistakably recognized this subconsciousness in his book the "World of Life" when he stated: "Immanent, directive, and organizing mind act on every living organism during every moment of its existence." The Century Dictionary gives the following definition of the soul: "a substantial entity believed to be that in each person which lives, feels, thinks, and wills. All animals, and even plants, have been thought to have souls."

Two of the most important properties of all life are perpetual and rapid internal motion and some trace of subconsciousness or consciousness, as I have previously pointed out. This "awareness" is found throughout the entire animal and vegetable kingdom; however, in the

1. Wallace, A. R.: The World of Life, New York, Moffatt, Yard & Company, 1911, p. 351.

lowest group of animals, viz., the Protozoa, as well as in plants, the intelligence is entirely subconscious and usually so slight as to be imperceptible, although it is undoubtedly present. Amoeba, which is merely a speck of jelly-like protoplasm, thrusts its legs (known as pseudopodia) out from its body to enable it to move about, and it encloses its prey inside them, drawing its stomach over it, for it is all stomach, so to speak. Professor Jennings, one of the most distinguished biologists in the United States, stated: "If an amoeba were the size of a dog instead of being of microscopic dimensions, no one would hesitate to ascribe to its actions the quality of intelligence." One has only to watch its hovering around a hydra when it is at the point of expelling a bud from its stalk, eagerly awaiting the juicy morsel in order to devour it, to be convinced of its subconscious intelligence.

The cells of the eyeball in the same way partake in some small degree of the intelligence of the entire animal, and therefore the eye cannot be treated as a dead organ. If one examines it one finds that it teems with life and energy and internal motion throughout its parts. The vitreous is no exception. Every part of the eye is composed of living cells which undoubtedly have a small amount of subconsciousness, which is shared with the entire human organism; in a certain sense the eye feels and is aware of what is going on and reacts accordingly, although the surgeon may not know it. Do not imagine for a moment that when a Graefe knife is plunged into the vitreous no harm is done and the cells of that part are not to some degree affected. When I was ophthalmic house surgeon my teacher used to say: "Be sure and do not excite or tease the part you are operating on or it will get angry and bite back." "Cet animal est très méchant, quand vous l'attaquez il se défend" [This animal is very vicious; when one attacks it, it defends itself] is a well known proverb.

One may think that the vitreous is merely a homogeneous jelly without soul or feeling. However, the moment one breaks through the so-called hyaloid membrane, whether with a knife or by some slight violence or pressure with the iris forceps, one disturbs a most intricate and complicated structure, consisting of a network of fine, transparent fibers, partly fused and partly containing between them a large number of lymph spaces which are throbbing with life and through which a stream of nourishment is continually flowing. Surgeons often state that one may allow a little vitreous to escape with impunity and that so long as the wound is closed no harm can result. But it is not the loss of a small amount of vitreous that does the harm but the changes set up through the disturbance of the vitreous structure. In certain cases of detachment of the retina von Graefe occasionally passed his knife through the vitreous and divided the retina across, but the ultimate

results were not encouraging, for the reason previously stated, and sometimes this procedure even led to destruction of the eye. The operation for the relief of glaucoma known as anterior sclerotomy, as practiced by Quaglino and improved by de Wecker, fell into disrepute for much the same reasons, and posterior sclerotomy was also eventually abandoned. To sum up, then, the practical point is that one must never touch the vitreous if it can be avoided.

ANATOMIC STRUCTURE OF THE VITREOUS AND HYALOID MEMBRANE

The intimate structure of the vitreous and the hyaloid membrane can be best studied with the microscope and a powerful beam of light thrown obliquely on to the vitreous by means of the slit lamp. Unfortunately, owing to its position, only a small part of the vitreous is accessible to the observer. But even in that case, to obtain a good view the pupil must be fully dilated with a mydriatic. Cocaine cannot be used for ophthalmoscopic examination of many animals, as for some reason, which I have never been able to determine, it causes bubbles to form inside the cornea which greatly interfere with definition. This is never the case in human beings; at least I have never observed it.

A few directions will be useful for the beginner in examining the interior of the eye by this method. The room must be made as dark as possible, and all extraneous light must be cut off. A blackened metal tube should be procured (a Koeppe's tube is excellent), but if a tube is not available, a couple of black cardboard diaphragms can be placed on the arm of the lamp. The slit should be fairly open, as a narrow slit cuts off too much light. The best form of illumination is undoubtedly the arc lamp, especially if the media are not perfectly clear and transparent. Moreover, one can narrow the beam of light to a much greater degree without cutting off too much light. It is best to commence the examination with a low power objective and eyepiece. A 16 mm. ⅔ inch.) objective and a Zeiss 2 ocular will suffice to begin with, and later for greater detail a 4 mm. apochromatic dry objective and a slightly higher ocular will be all that is required. A high power objective with a low ocular gives a much better definition than a low objective and a high eyepiece with the same magnification.

One begins by focusing the instrument on the posterior capsule of the lens. This can be recognized by the brilliant luster of the central parts. One should be sure to dodge the light so as to get rid of all reflexes. The fetal sutures which form an inverted Y close to the posterior capsule are first brought into focus. The center of this Y shows the exact center of the lens along the visual axis. If the beam is moved slightly toward the nose, a curved line can be noticed which

forms a portion of a circle just on the inner side of the Y (in the right eye), with its convexity toward the Y. This is known as "Vogt's arcuate line." Inside this curve, just where the chord of the arc would lie, is a large bright hyaloid corpuscle, which is quiet and transparent. To this a long thread twisted like a minute worm is attached, which with the slightest movement of the eye wriggles about as if it were alive. This threadlike body is the vestigial relic of the fetal hyaloid artery, which has almost entirely disappeared in man, although in many of the Ungulata, especially in all the species of the Cervidae (antelopes), it will be found to be a permanent structure and can be readily seen as a bifurcating cord with the ophthalmoscope. In man, only Vogt's line can be seen outside the zone of specular reflection.

Immediately behind the capsule is a shallow space known as the retrolental space or patella. Here the capsule of the lens is prolonged into a narrow tube, which gets smaller and smaller, until it becomes contracted into a cord; when it reaches the center of the optic nerve it again widens. This tube cannot be perceived by the ophthalmoscope except in rare instances, but it can usually be traced a little way by means of slit lamp illumination. For the purpose considered here it has no significance.

Everywhere, according to Berger, the capsule of the lens is separated from the hyaloid membrane by a narrow lymph space, except at one point known as Egger's line, which forms a distinct line or ridge where the zonule or suspensory ligament is attached to the angular border of the capsule of the lens. This line may be demonstrated clinically when it prevents blood behind the lens from spreading forward. The line varies in thickness from 0.25 to 0.75 mm. in some cases. It measures the width of attachment of the zonule to the capsule. I shall consider it in detail when I describe the zonule.

Examined by the slit lamp method, I found that the vitreous is highly luminous, owing to the large molecules of colloid jelly which reflect sufficient light to give it a slightly opalescent tinge. One can readily see the aforementioned postlental space by the vertical reflex which defines the anterior limiting membrane or layer of the framework of the vitreous. Around this space one can perceive a collection of filiform threads, which appear twisted together and joined on in places. These threads, which are nearly transparent, are the vestiges of the vasa hyaloidea of Schultze. Seen with the slit lamp and microscope, the entire vitreous appears to be composed of an immense network of coarse fibers, resembling coconut matting tissued out, and a large number of fibers of much finer texture which cross the coarse fibers obliquely. As a person advances in years, the fibers gradually change in appearance and become broken up into dots, or "peppering," as they are sometimes called. This is markedly the case when the vitreous

becomes degenerated around the age of 70. The fibrillar structure cannot be seen in perfectly fresh vitreous with the help of a loupe (simple lens magnifier) or even with a compound microscope but it can be seen with the slit lamp and microscope. According to the late Professor Gullstrand, it appears as a series of membranes having a netlike structure arranged both vertically and horizontally. This, however, has been denied by Duke-Elder, Heesch and others, who state that the picture is optical rather than anatomic.

The aqueous cannot be considered as a part of the living structure of the eye as is the vitreous, since it is composed of merely water with a minute quantity of mineral salts. Nothing one can do to it can affect the eye in the same manner as do surgical procedures on the vitreous. Moreover, a clean cut, such as is made with a keratome or in taking out a piece of the iris, cannot do appreciable harm. For the same reason, a clean cut made by a punch at the sclerocorneal junction for glaucoma will cause far less irritation and subconscious disturbance to the eye, as well as to the whole body, than a perforation made by a gimlet, as in Elliot's operation with a Stephenson trephine.

CHEMICAL NATURE OF THE VITREOUS AND HYALOID MEMBRANE

All colloids, of which the vitreous is a perfect example, exist in two forms called sol and gel.

The sol, or soluble form, is one in which the colloidal molecules move freely in water and thus form a typical solution, whereas the gel variety has a high viscosity as well as some rigidity and elasticity, so that instead of being a solution of a colloid in water it becomes a solution of water in a colloid. If sufficient water is evaporated, the swollen fibrillae of ultramicroscopic size gradually form a fine film or felt of long, white fibers and a kind of curd or soap (the coagel of Laing).

SO-CALLED HYALOID MEMBRANE

In a communication read before the American Ophthalmological Society in 1931, Cowan [2] stated that a definite membrane could be demonstrated on slit lamp examination in every eye after removal of the lens for cataract, provided no complications ensued. In a subsequent communication Cowan and Fry [3] endeavored to present both

2. Cowan, A.: Concerning a Membrane Between the Vitreous and the Anterior Chamber, Seen After Removal of the Crystalline Lens and Its Capsule, Tr. Am. Ophth. Soc. **29**:179, 1931.

3. Cowan, A., and Fry, W. E.: The Hyaloid Membrane of the Vitreous, Arch. Ophth. **7**:340 (Feb.) 1932.

anatomic and histologic evidence that such a membrane exists in all mammalian eyes which they had examined (pig, monkey, kangaroo and human eyes). They expressed the belief that a definite, nonmolecular, structureless, uniformly staining membrane exists which completely separates the aqueous from the vitreous chamber, that this membrane is normally in contact with the posterior lens capsule and that it may be called the anterior hyaloid membrane of the vitreous. On the other hand, other equally able observers have failed to identify this membrane, and the general opinion in the discussion which followed the paper by Gowan and Fry was that this membrane was purely the result of the hardening effect of fixative agents and alterations due to stains used to demonstrate the membrane; however, to my mind the evidence of the existence of this membrane is completely nullified by the chemical changes which take place whenever a colloid solution is exposed to the air or forms a boundary surface. These changes have already been discussed, and they appear to account perfectly for the supposed membrane which Cowan and Fry photographed and prepared with such extreme care. Of course, one cannot absolutely deny the existence of the membrane, but the chemical evidence is surely against it. One thing is certain, and that is that the slightest prick or pressure of the knife or forceps or even a spatula will break through this so-called membrane into the vitreous and cause the latter to escape, but merely stroking or gently pressing on the membrane with the flat surface of the spatula will not be sufficient to cause it to rupture, and one can put a considerable amount of pressure on its surface with any smooth flat instrument without the slightest fear.

Duke-Elder in his standard work on ophthalmology stated without any reserve that there is no membrane either behind or in front of the vitreous. According to him, the so-called membrane lining the posterior part of the vitreous belongs to the retina and forms its innermost layer. He further added that the surface of any colloid invariably becomes condensed on exposure.[4] In addition he stated:

> The skin which is formed on the surface of boiled milk is a well-known example of an extreme case [of condensation]. It may be considered to originate somewhat as follows: The colloidal particles are in the first place adsorbed on the surface, where, being tightly packed and closely crowded together, the micellae become oriented in parallel lines and are eventually coagulated. . . . Condensation of such a nature plays a very important part in cell division, and it undoubtedly takes place at the internal and external surfaces of the vitreous body, and gives rise to the optical appearances and the histological coagulum which have been described as a hyaloid membrane.

4. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1933, vol. 1, p. 117.

THE ZONULE OF ZINN

This description of the zonule of Zinn is chiefly taken from Duke-Elder's textbook,[5] as it is the only complete description I could find; indeed, most textbooks say next to nothing about it.

In a fresh eye examined immediately after removal the zonule appears as a thick, band-shaped structure attached above to the equatorial region of the lens. The anterior surface runs straight from the capsule of the lens to the anterior surface of the ciliary processes and from the posterior boundary of the posterior chamber. The length of the zonule varies from 2 mm. in a child to 0.5 mm. in an elderly person. In many cases the zonule comes in direct contact with the ciliary processes, so that in such cases it can hardly be said to exist as a membrane. The posterior surface is curved, bending along the inner surface of the ciliary body as far as the ora serrata, and it is separated from the front surface of the vitreous by a small space, the canal of Petit. Both surfaces have a glistening appearance and show marked striations, running in a general direction from the lens to the ciliary body; this appearance is demonstrated clearly when one puts traction on the lens. The striations appear to be made up of delicate strands of the same fluid as is found in the vitreous; in other words, the zonule of Zinn is made up of vitreous fluid, between which a homogeneous transparent gel is placed. If this is really the case, it is difficult to understand how this strand of vitreous jelly can stand the constant pressure which Helmholtz makes it bear until it is relaxed by accommodation. The space between the two surfaces shows an irregular crisscross of similar strands, among which lies a much more fluid and perfectly homogeneous gel-like material. Through this gel, fluid diffuses with ease from the vitreous into the anterior chamber. Duke-Elder stated:[6]

> . . . recent work, however, has shown . . . that the zonule is merely a differentiated portion of the vitreous in which the appearance of fibres is an artifact of histological technique. Consequently, the posterior chamber is best defined as the space bounded in front by the iris, and behind by the anterior surface of the lens and the anterior face of the zonule.

5. Duke-Elder,[4] p. 131.
6. Duke-Elder,[4] p. 82.

SEASONAL VARIATIONS IN LIPID CONTENT OF CRYSTALLINE LENSES

WITH SPECIAL REFERENCE TO THE INFLUENCE OF SUNSHINE AND HUMIDITY

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In a previous study [1] on the seasonal variations in the lipid content of crystalline lenses, there appeared during the course of a year two low and two high levels in the lipid content. The low levels coincided with the spring and the fall and the high levels with the summer and the winter. The variations were more pronounced on the basis of per cent than on the basis of absolute amount, indicating simultaneous but inverse changes in some other substance, apparently water. Certain seasonal changes were noted also in the cholesterol and phospholipid contents of two other groups of similar lenses, the values for cholesterol being especially high during the winter months and those for phospholipids during the summer months. By summation of the two lipid fractions, a curve was obtained that closely resembled that for the total lipid. At that time no study was made regarding the precise influences responsible for the aforementioned changes. It was thought, however, that the ultimate causes lay chiefly in such factors as sunshine, temperature and humidity. In order to find out whether this supposition was correct, the present study was undertaken.

In all, 267 cataractous human lenses were analyzed separately for both total lipids and cholesterol. The values for total lipids were estimated gravimetrically by a previously described procedure.[2] For the determination of cholesterol Bloor's colorimetric method [3] was used. The results are expressed in relation to the wet weight of the lens tissue. Although the lenses were cataractous, this condition, as was

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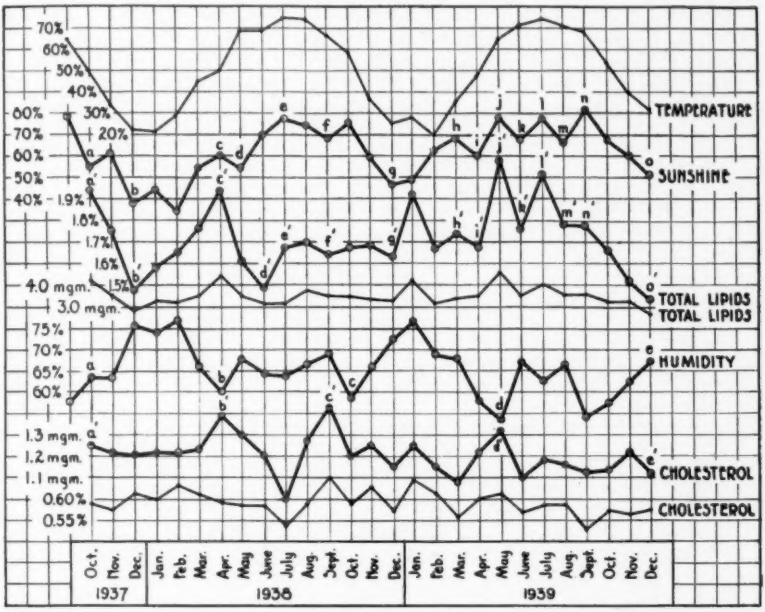
1. Salit, P. W.: Seasonal Variations in the Lipid Content of the Crystalline Lens, Arch. Ophth. **18**:403-410 (Sept.) 1937.

2. Salit, P. W.: Total Lipids of Human Cataractous and Sclerosed Lenses, Am. J. Ophth. **20**:157-165, 1937.

3. Bloor, W. R.: Studies on Blood Fat: II. Fat Absorption and the Blood Lipoids, J. Biol. Chem. **23**:317-326, 1915; The Determination of Small Amounts of Lipid in Blood Plasma, ibid. **77**:53-73, 1928.

explained in detail in an earlier publication,[1] has practically no effect on the accuracy of the results. The patients from whom the lenses were obtained were residents of Iowa. Their ages varied between 45 and 88 years, with an average of 69.3 years. The number of lenses obtained each month varied between 3 and 17. The study extended over a period of twenty-seven months, beginning with October 1937, and ending with December 1939. The results were studied in relation to variations in the atmospheric conditions in Iowa as reported for that period by the weather bureau of the department of agriculture at Des Moines.[4] The



Changes in the total lipid and cholesterol content with relation to temperature, sunshine and humidity.

special phases of weather conditions referred to in this study are temperature, sunshine and humidity.

As may be seen from the accompanying chart, the total lipid content of the crystalline lenses, in agreement with previous findings, showed certain definite variations during the twenty-seven months. These variations, like those reported previously,[1] were much more pronounced on the basis of per cent than on the basis of absolute amount. But temporally, i. e., with relation to the four seasons of the year, the changes in the lipid content in the present study did not coincide with those reported earlier.

4. Reed, C. D.: Climatological Data, U. S. Department of Agriculture, Weather Bureau, Iowa Section, Des Moines, Iowa, October 1937-December 1939.

Therefore, the different seasons of the year in themselves are not the determining factors in the observed changes in lipid content. From the accompanying chart it is seen that the sunshine curve resembles more closely the total lipid curve than do the temperature and humidity curves. With the exception of one irregularity, falling in January 1939, the total lipid curve follows the sunshine curve practically in every particular, as is shown by the partial curves *ab-a'b'*, *bc-b'c'*, *cd-c'd'*, *de-d'e'*, *ef-e'f'*, *fg-f'g'*, *gh-g'h'*, *hi-h'i'*, *ij-i'j'*, *jk-j'k'*, *kl-k'l'*, *lm-l'm'*, *mn-m'n'*, and *no-n'o'*. The magnitudes of the changes in the curve for total lipids, however,

Seasonal Variations in the Total Lipid and Cholesterol Content in Human Crystalline Lenses

Year	Month	Number of Lenses	Average Age of Patients	Average Amount of Total Lipids		Average Amount of Cholesterol	
				Mg. per Lens	Per Cent	Mg. per Lens	Per Cent
1937	October	10	72.2	4.1	1.940	1.240	0.587
	November	12	70.6	3.6	1.762	1.212	0.571
	December	9	65.1	2.9	1.470	1.206	0.612
1938	January	10	70.6	3.3	1.586	1.232	0.597
	February	8	66.6	3.2	1.660	1.219	0.632
	March	8	71.9	3.5	1.764	1.228	0.610
	April	16	73.1	4.5	1.942	1.376	0.595
	May	7	72.4	3.5	1.606	1.290	0.587
	June	4	68.3	3.1	1.480	1.198	0.591
	July	7	73.3	3.1	1.684	0.990	0.534
	August	11	75.2	3.7	1.694	1.271	0.593
	September	3	68.7	3.6	1.640	1.432	0.650
	October	15	66.5	3.4	1.660	1.197	0.593
	November	8	68.5	3.4	1.680	1.253	0.629
	December	10	68.0	3.3	1.632	1.148	0.570
1939	January	6	65.3	4.1	1.928	1.258	0.644
	February	6	62.8	3.2	1.661	1.155	0.614
	March	10	65.4	3.4	1.727	1.078	0.558
	April	10	68.7	3.5	1.676	1.215	0.599
	May	11	70.4	4.6	2.089	1.330	0.609
	June	7	67.9	3.5	1.761	1.100	0.570
	July	13	67.1	4.0	2.016	1.174	0.590
	August	6	70.9	3.6	1.784	1.158	0.592
	September	16	66.8	3.6	1.782	1.115	0.533
	October	13	70.2	3.2	1.658	1.135	0.575
	November	17	70.4	3.3	1.505	1.210	0.564
	December	13	69.0	2.8	1.420	1.120	0.576

are not always exactly proportional to those of the corresponding changes in the curve representing sunshine. Nor do the two corresponding points *d* and *d'* fall in the same month. These more or less insignificant deviations must be attributed to secondary influences, such as temperature, humidity, diet and mode of living, as well as the fact that sometimes the entire monthly collection of lenses was obtained within either the first or the last week of the month and thus was not fully representative of that particular month. Nor are the sunshine averages, for the same reason, always fully representative of the months for which they are given. Thus two temporally corresponding points on two related curves may be found an entire month apart.

The variations in the cholesterol content are more pronounced on the basis of the absolute amount than on the basis of per cent. A definite inverse relation between the cholesterol curve and the humidity curve is indicated; the cholesterol content decreases with increase in humidity, and vice versa. The inverse relation between the two curves, as shown by the partial curves *ab-a'b'*, *bc-b'c'*, *cd-c'd'* and *de-d'e'*, is as striking as the direct relation between those for total lipids and sunshine. The slight irregularities must be accounted for in the same way as those between the total lipid and sunshine curves.

According to a previous publication,[1] as was pointed out at the beginning, there is a tendency for the phospholipid content of the crystalline lenses to vary inversely with the cholesterol content. Therefore, one would expect the phospholipids to vary directly with humidity. This is in harmony with the fact that the phospholipids are especially known for their hydrophilic properties, whereas the cholesterol is known to be hydrophobic. The former must be associated, therefore, with high and the latter with low moisture content of the tissues. Consequently, they must be associated also with temperature changes of the body in which they may play an important role as temperature regulators.

SUMMARY

The total lipid and cholesterol contents of 267 human cataractous lenses were studied over a period of twenty-seven consecutive months. The lenses were obtained from persons whose ages varied between 45 and 88 years, with an average of 69.3 years. All patients were residents of Iowa. The results were plotted against temperature, sunshine and humidity as reported during that period for the state of Iowa by the weather bureau of the department of agriculture at Des Moines. There were definite variations in both the total lipids and cholesterol contents, those of the former being more pronounced on the basis of per cent and those of the latter on the basis of the absolute amount. The total lipids varied directly with sunshine; the cholesterol varied inversely with humidity. On the basis of the present results as well as those of a similar, earlier study, it is concluded that the inverse relation of the cholesterol to humidity represents a phase of a bipolar chemicophysiologic system in which the phospholipids represent the opposite phase. The phospholipids therefore would be expected to vary directly with humidity. Such a chemicophysiologic system, in which one of the chemical factors is hydrophobic and the other hydrophilic, the two varying inversely to each other according to the moisture content of the atmosphere, must have something to do with the water transportation and consequently also with the temperature regulation of the tissues.

OCULISTS AND OCCULTISTS

ASTROLOGY AND THE EYE

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The idea that disease is caused by occult powers was rooted in the mind of primitive man from time immemorial. The supernatural forces responsible for morbid conditions were believed to have taken their origin from four different sources: (1) subterranean powers, such as ghosts of the dead; (2) terranean forces, such as the evil eye; (3) aerial agencies, such as demons and elves, and (4) heavenly powers, such as gods and stars. The present paper is confined to the subject of healing through the stars, with special reference to the eye.

"When God created the universe he set in motion the two great lights. When he created man he placed in him two eyes" (Emerson).

To the ancients, the analogy of the human eyes to heavenly bodies was not merely metaphoric. Hermes Trismegistus, often styled "The Father of Egyptian Medicine," following the Egyptian doctrine that each organ of the body is controlled by a deity, stated that the sun god rules the vision of the right eye and the moon god controls the function of the left eye. The remainder of the thirty-six parts into which the body was divided was placed under the influence of the planets. This occult system of medicine, cultivated in Egypt and Mesopotomia, was taken over by the Greeks, who broadened its scope and developed it into a philosophic system, embracing all the sciences.

The ancients considered man a universe in miniature (microcosm), molded by the creator after the larger world (macrocosm) and composed of the same elements and physical characteristics (fig. 1). The eyes were conceived as corresponding to the greater lights of the macrocosm. Whereas it is true enough that the macrocosm or nature has a powerful influence on human life and activity, the rude philosopher considered this influence to be metaphysical. He believed that every organ of the body was completely controlled by the planets, which were capable of operating favorably or unfavorably as they willed. He felt certain that man's destiny as to health and disease is dictated by a particular planet or the god represented by the star.

This article is the third and last of a series on occult sciences in their relation to the eye. The first, entitled "Oculus Fascinus (Fascination, Evil Eye)," appeared in the February 1937 issue of the ARCHIVES (page 290). The second, "Oculists and Occultists: Demonology and the Eye," appeared in the July 1939 issue of the ARCHIVES (page 25).

Astrology was one of the most destructive notions in the history of medicine. Unlike other medical fallacies, which attributed the cause of disease to supernatural forces, sidereal medicine ascribed the etiology of disease to natural occurrences, such as the arrangement of the heavenly bodies at the time of birth or at the period when the patient took sick.

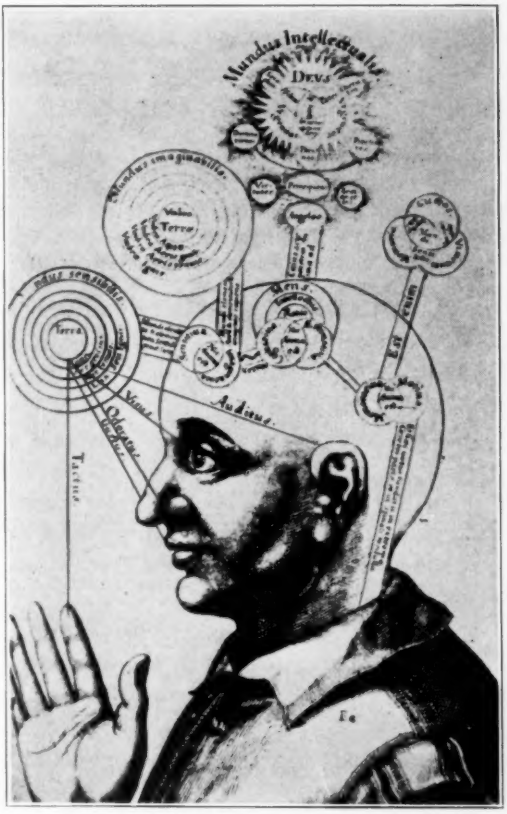

Fig. 1.—The conception of "The Great Man" (Adam Kadmon) of the heavens as pictured by Robert Fludd (1619) in his "Microcosmi Historia." A clear demonstration is given of the three kinds of vision in the microcosm (or soul of man), of the location of their objects and the manner of discerning them. (From Kenton, E.: Book of Earth, New York, William Morrow & Co., Inc., 1928.)

Because of its scientific pretenses, astrology attracted not only the ignorant and credulous masses but even the well informed and cultured elements. By dialectic methods and fanciful calculations, astrologic medicine took under its wing many medical theories. Thus, for example, the humoral theory of Hippocrates, which postulated as the cause of disease the improper combinations of the four principal humors, became

associated with the system of sidereal medicine, on the supposition that a particular star dictated the hour of the day or night on which the flow of humors was to cease. The atomic theory of Epicurus, that disease is produced by the inhalation of particular kinds of atoms or seeds into the system, was interpreted astrologically on the basis that inhalation of the atoms was influenced by the ascending star at the time of birth.

CHALDEA, THE CRADLE OF ASTROLOGY

That Chaldea was the cradle of astrologic observation is well known. As Mellvile eloquently expressed it:

> On the wide stretching plains of Western Asia, in the warm cloudless Assyrian night, with the lamps of heaven flashing out their radiance in uninterrupted splendor from the center to the boundless horizons, it was no wonder that students and sages should have accepted for their deities these destined worlds of fire on which eyes, brain, hopes, thoughts, and aspirations were nightly fixed.

"As the lives of the Chaldeans were largely influenced by a change in the seasons," said Maspero (1846- ——) in "Dawn of Civilization," "they laid great stress upon division of time." In the beginning they probably based their chronology on the movement of the moon. Soon they recognized that the sun exerted a strange influence, and accordingly they introduced a solar year the division of which they ascribed to Marduk. The stars were observed because their position determined the seasons. Since the seasons govern organic life, a pernicious belief in the influence of the stars took root, a belief that crippled the advance of science up to the time of Galileo.

The primitive belief that everything that moves has a spirit or is a spirit itself endowed the moving planets in the heavens with the status of godhood and transformed astronomy into astrology and priests into astrologers.

The Chaldean priests mapped out the position of the stars for every day. They could tell their position for some time in advance. If, therefore, a Chaldean king wished to know which star ruled over his destiny, he consulted the priests as to the position of the stars on his birthday and was informed of the chief future events of his career. Subsequently, the scope broadened to include the prediction of the future of all persons and even of animals and things.

The names of the seven heavenly bodies, in the order they appear in the cuneiform literature, are as follows: Shamash (sun god), Sin (moon god), Marduk (identified with Jupiter), Ishtar (identified with Venus), Ninib (identified with Saturn), Nebo (identified with Mercury) and Nergal (identified with Mars). These divinities were believed to control all the manifestations of nature.

The information derived from these planets was known by the ancient world as the "Chaldean wisdom." In the movements of the sun, moon and five planets were recognized the intentions and purposes of the gods; thus future occurrences on the earth were predicted, and man was able to govern his actions accordingly.

Long before the "high towers" of the temples of Babel were erected, whence the royal astronomers sent their reports to the kings, the leading stars had been known to the Babylonians and to the kindred nations of Mesopotamia. The heaven was already divided into twelve sections, each distinguished by its chief constellation. The zodiacal circle was already drawn. A calendar was devised for the entire year, and records of the eclipses of the sun and moon, as well as the annual revolution of the sun as it passed through the sky, were noted. Inscriptions from remote antiquity show that the zodiacal circle was included in Accadian calendars.

Tradition attributes to the Assyrian king Sargon [1] (late eighth century B. C.) a compilation of a standard work on the observations of Bel (astronomy and astrology), which was translated into Greek by Berossos.

The knowledge of the heavenly bodies presupposes an advanced status of astronomic observations. It would have been impossible to make astrologic calculations, to devise a calendar for the year and draw the zodiacal circle without a basic knowledge of the heavenly bodies. It was, however, astrology and not astronomy for which the Babylonians can claim credit.

The Jews appropriated the Chaldean conception of the universe but so modified it that it was transformed from a polytheistic to a monotheistic conception. In the days of Moses, the belief in astrology was widespread in Egypt. Jewish tradition relates that Pharaoh ordered the midwives to drown all Hebrew male children only after his astrologers had told him that a future redeemer of Israel was to be born.[2] The Book of Judges, describing the victory of Sisera, states: "They fought from heaven; the stars from their courses fought against Sisera." [3]

Classical Hindu writers, Garga, Parashara and Mihara, as well as their numerous commentators, give much space to astrologic speculations.

Chinese rulers, as far back as the twenty-second century B. C., attached great importance to sidereal phenomena. It is recorded in the historical classics of China that the court astrologers Hi and Ho were deprived of their offices, had their estates confiscated and were

1. Isaiah **20**:1-4.
2. Talmud: Sanhedrin 10b.
3. Judges **5**:20.

driven from the kingdom because they failed to foretell a solar eclipse that took place at Peiping between 7 and 9 a. m. on Oct. 10, 2154 B. C. This neglect of duty created the utmost consternation in Peiping and caused the people to run about in wild confusion.

A VAGUE CONCEPTION OF THE UNIVERSE

Early man in Western Asia was prompted to associate his personal fortune with the heavenly bodies by reason of his vague conception of the universe (figs. 2 and 3). He fancied the earth which he inhabited to

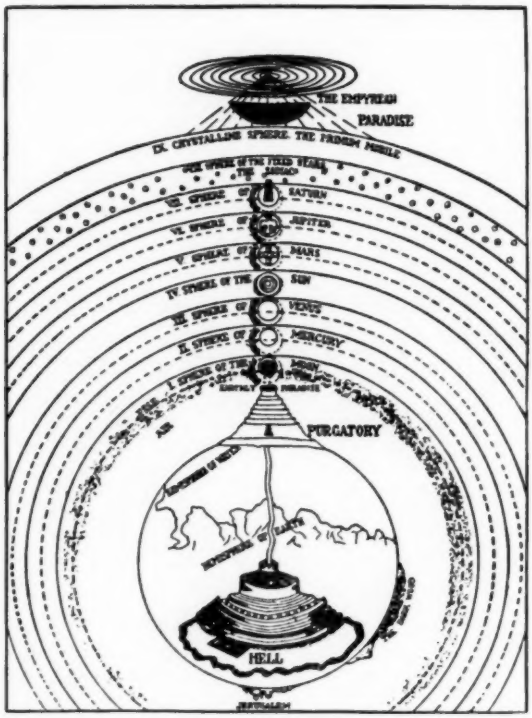

Fig. 2.—Dante's scheme of the universe slightly modified by Michelangelo Caetani, showing the nine heavens and the planets and paradise and hell. The earth is described as an inverted cone descending in nine diminishing whorls through the hemisphere, which is also the center of the universe and is situated just under Jerusalem, the center of the habitable earth. The nine spheres are each occupied by the planets and stars. (From Singer, C. J.: Studies in the History of Method of Science, New York, Oxford University Press, 1917.)

be hollow, of small dimensions and covered by an arched sky that was so close that it could be reached by a high tower. He pictured the earth to be encircled by a high wall, and the abyss between the earth and the wall

to be filled by the ocean (fig. 4). Beyond this wall was the abode of the immortals. The walls built by Marduk supported the vault of the firmament. Early man also conceived of a nether world—a basement of the earth as it were. In other words, he visualized a little three story world. In the most spacious apartment, the sky, he placed the gods. To the basement (*sheol*) he assigned the spirits of the dead, and the intervening compartment he allocated for himself. His cosmic mansion was provided with lamps, the sun and moon—"the greater light to rule the day and the lesser light to rule the night." The stars he considered as a kind of auxiliary lighting system, a mechanism provided in the event the main

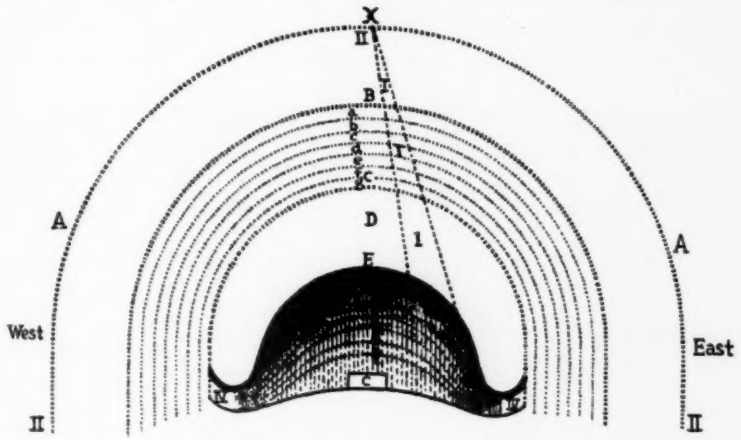

Fig. 3.—Myer's construction of the Accadian, Chaldean and Babylonian conception of the universe. They considered the earth to be hollow. *E* represents the convex side of the hollow earth shell. From *C* to *E* stretches the lower firmament, or zone of the atmosphere—winds, storms and clouds; this zone rests on the convex side of the earth's shell. The upper firmament is divided into two layers, from *C* to *A*. The zone of the spirit of the heavens is shown between letters *A* and *B* and the zone of the planets from *B* to *C*. The *B* to *C* zone is also the zone of lightning and thunder. *A* represents the zodiac, which is "in space and the great celestial ocean"; it was called also the "deep" and "abyss." *F* and *F* is the concave side of the earth's shell. This was thought to be the realm of the king of the ghost world. *G* represents the Nadir, and *I*, the mountain of the world which supported the upper firmament and the celestial ocean. (From Qabalah: Isaac Meyer, 1888, reproduced by Kenton, E.: Book of Earth, New York, William Morrow & Co., Inc., 1928.)

power plants failed, as in an eclipse, or when the moon absented itself from the sky during the latter part of the month.

As time went on, it occurred to early man that the sun had other uses besides serving as a lamp. He noticed that it possessed various beneficial and detrimental attributes; that, on the credit side, the sun had a wholesome influence on his own life and the lives of his animals

and plants. On the other hand, during the rainless summer the sun was responsible for the seasonal sterility and devastation.

The moon also exerted a powerful influence on the man of antiquity. The moon was the guide of the ancient nomad who roamed the wastes of his unexplored land and furnished the only means of calculating the time of the month, the week and approximately the hour of the night.

The first stargazers had no knowledge of optics, physics or meteorology. They did not know that the regular spherical form of the sky is an effect of perspective. They were ignorant of the fact that the blue of the firmament is a subjective phenomenon caused by the light traversing the atmosphere before it strikes the retina, and they did not realize that the winds, clouds and northern lights are terrestrial phenomena related to astronomy but distinct from the signs of the heavens.

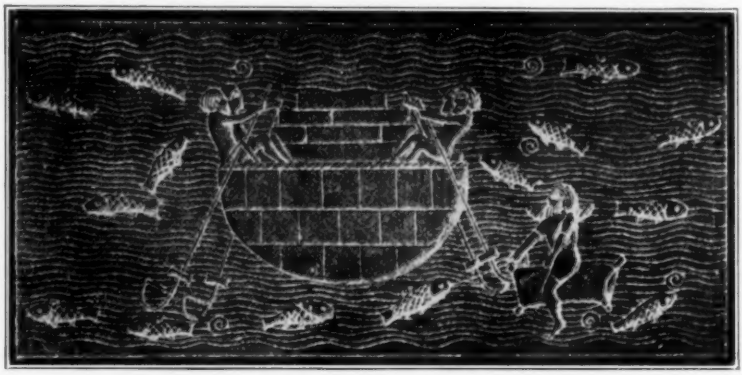

Fig. 4.—Another diagram of the Accadian universe, showing the kufa, a little floating world manned by a crew of four men. (Drawn by Faucher-Gudin from a bas-relief of Ninveh; taken from Maspero, G.: Dawn of Civilization, 1894.)

Xenophanes was among the first of the Greek sages to expound the connection of the stars with the earth. His teaching that the stars were meteors (terrestrial effluvia) was the basis of astrologic development among the Greeks and the Romans.

Early Greek mythology is inextricably bound up in a complex system of cosmographic astrology. The Greek mythical heroes were always guided by the heavenly constellations. Astrology in Greece reached the peak of its popularity in the fourth century B. C.

Under the erudite Greeks, astrology passed beyond the limits attained by the Babylonians. The phenomenal advance of the Greeks in the pure sciences did not prevent them from developing the pseudoscience of astrology. By a curious process of combination and a strange association of ideas, the entire realm of natural science was translated into astrologic language, and astrology became bound up with all known

sciences, such as botany, chemistry, zoology, minerology, anatomy and medicine. Aristotle made it a part of his philosophy. Hipparchus, Hippocrates, Thales and Galen subscribed to some of its principles.

Claudius Ptolemy (—— - 162 B. C.) was the first writer to give a concise and systematic treatment of the doctrine of astrology. In his "Tetrabiblos" (four books), he laid the foundation of the so-called astrologic science. He was supported by another Greek scholar, Julius Firmicus.

The discoveries of the planets Uranus and Neptune by Herschel and Adams, respectively, almost overturned the whole system of Ptolemy and his followers, for their doctrines were based on the assumption that the earth does not move and that there are no more than seven planets in the solar system. Thanks to the dialectic methods and hair-splitting reasoning in vogue, a way was found to keep astrology alive.

For three millenniums the terms *astrologia* and *siderari,* as used by the Greeks and Romans, explain all unknown natural phenomena and particularly morbid conditions in man. Indeed, this idea prevailed until the eighteenth century, when an English philosopher tried to prove that epidemics are due to the shock of comets.

OBSERVATIONS OF THE HEAVENLY BODIES

But while the Greeks and Romans furnished the rationale, the basis of astrologic belief was laid by the Chaldeans who, while gazing at the canopy of heaven in the course of their daily toil, made and recorded numerous observations of the "hosts of the heaven."

In the case of the moon, for example, the Chaldeans observed the monthly changes in its shape and position, the exact appearance of the new cresent, its position in the heaven, its conditions, such as conjunction and opposition, the appearance of the horns, the halo frequently seen with the new moon (which was compared to a cap), the time of the month the moon appeared, the ring around the full moon (which was called a stall or enclosure) and such other phenomena as were painstakingly noted. Greater significance was attached to more striking phenomena, such as when an eclipse of the moon took place. Similar observations were later applied to some of the fixed stars and constellations.

Interpretations were based principally on two factors, old chronicles and tradition. Thus, for example, if an Assyrian war with Shinar had followed the eclipse of the sun, it was supposed that a recurrence of an eclipse on the same day would be followed by a recurrence of the war; and if an epidemic of plague or of ophthalmia followed a thunder storm soon after sunrise on a certain day, it was assumed that the recurrence of such a storm on that day would be followed by a recurrence of the same epidemic.

Again, if it was found in old chronicles that on a certain occasion the sudden disappearance of the moon was followed by a catastrophe, any similar disappearance would be taken to be a bad prognostic sign. Or, if in the memory of certain persons the appearance of the new moon earlier than expected was followed by sickness or death, repetition of this was taken as a bad omen. On the other hand, if the rise of the new moon in a cloudy sky was followed by rain or by the birth of a male child, or by success of a certain enterprise or by recovery from a troublesome disease, the sign in question was considered favorable and was regarded as a good omen. The thin halo seen above the new moon (pictured as a cap and looked on as a symbol of royalty because of its conical shape) was interpreted as a sign that the country would be successful under the new ruler.

The Chaldean priests, who also occupied the position of astrologers, not knowing the causes of events, assumed that when two events happened one after the other, the first was the cause of the second (*post hoc ergo propter hoc*).

Both through personal observations of the heavenly bodies and by following the records of the priests, the students of astrology learned sidereal methods of prognosticating the future of disease as well as of other happenings. It is obvious that such predictions most often did not materialize; but the sun and moon were divine entities, and unfulfilled prophecies concerning them were attributed to divine will.

In such fasion a mass of traditional interpretations of all kinds was gathered and became a guide to astrologers for all times. It is apparent that the observations noted must have grown in the course of time to large proportions and that, correspondingly, the interpretations assigned to them must have also grown enormously. It was generally interpreted that variations from the usual phenomena were efforts on the part of the gods to communicate with man and tell him what was in store for him. It was not an easy task to make silent gods talk, so methods of sophistry, hair-splitting argumentations, strange association of ideas and forced analogies were brought into play to effect this end.

NATURE WORSHIP

The sun was worshiped by many nations of antiquity. As early as five thousand years ago the sun was worshiped in Mesopotamia as the god of the universe. Hammurabi, the king of Babylonia, is pictured as standing before the sun god Shamash while receiving his legal code. The Egyptian Pharaohs claimed origin from the sun god Ra. The Chinese paid homage to an idol representing the sun. The Japanese worshiped the sun, which was depicted as a feminine deity from whom their Mikados were descended. In Japanese mythology the sun and moon gods were formed from the eyes of their progenitor.

Although Moses prohibited all kinds of nature worship,[4] the kings of Judah dedicated horses to the sun.[5] Ezekiel saw twenty-five men at the door of the temple worshiping Shemesh.[6] That sun worship in Palestine must have been popular can be seen from the fact that four cities (Beth-Shemesh, Mount Heres, Ein-Shemesh and Kir Heres) were dedicated to Shemesh. These cities probably existed before the Israelites entered Palestine, for the Scripture prohibits the worship of Shemesh.

To this day some American Indians believe that the sun and all heavenly bodies are animate beings, possessing a vitalized soul and a large measure of intelligence. Since they believe that the sun is not merely the agency of God but is the living God, sun worship is never performed symbolically (as if the sun were the representative of some invisible or absent spirit) but directly (as if the sun were the very embodiment of the divine). Paying homage to the sun is still practiced in certain Arctic sections. The people of Hammerfest celebrate the return of the sun to that Arctic city with festivals and rejoicing.

The Book of Malachi attributes the process of healing to the sun in the following metaphor: "but into you . . . ," said the prophet, "shall the sun of righteousness arise with healing in his wings." [7]

The sun was not always a benevolent god. It frequently punished persons with disease. Many ocular diseases prevailing in the tropical east, such as trachoma and other forms of ophthalmia, were attributed to the direct action of the sun.

Moon worship was even more popular in antiquity than sun worship. The people of Mesopotamia worshiped the moon (Sin) as a male deity.

The moon god was frequently referred to by the Egyptians as Isis and was one of the two deities most revered by the Egyptians. The Egyptians sometimes represented the moon god as possessing a man's face with the crescent of the moon on his head.[8] Plutarch stated the Egyptians frequently called the moon "the mother of the world" and held it to be of both sexes, female as it is influenced by other gods and male as it scatters and disperses through the air the principles of fecundity.

The moon was described as possessing both generative and destructive faculties and was worshiped as a good and as a bad power. The Egyptians sacrificed swine to the full moon, although swine were con-

4. Deuteronomy **4**:19.

5. II Kings **23**:11.

6. Ezekiel **8**:16.

7. Malachi **3**:20.

8. Wilkinson, J. G.: Ancient Egyptians, New York, Harper & Brothers, vol. 2, collection 5, 1854.

sidered impure and forbidden as an offering to other deities. According to Herodotus, the moon god and Bacchus were the only deities to whom swine were sacrificed in Egypt.

In India the moon god was known as Maja and in Syria as Mylitta. Karnaim, often referred to in the Old Testament, means "horns" in Hebrew, an analogy being drawn between the crescent-shaped moon at the early part of the month and an animal's horns.

The moon was associated with many diseases. According to eastern belief, blindness, epilepsy and insanity are produced by prolonged exposure to the moon. The word "lunatic" is derived from *luna* (the moon). The Psalmist referred to "sun stroke" and "moon affection" when he stated "the sun shall not smite thee by the day, nor the moon by the night." [9] To this day Arabs of the Near East ascribe various forms of ophthalmia to prolonged exposure to the moon.

Although, as pointed out previously, the Hebrew scriptures are against all forms of nature worship, Ashtoreth (or Astarte), the Canaanite mother goddess, was nevertheless popular in Judah until the exile. Moon worship in Palestine was particularly popular during the reign of Manaseh. It is said that this monarch worshiped "all the hosts of heaven." [10] Josiah subsequently destroyed these idols, and the priests who burned incense to the moon were also put down." [11]

Isaiah rebuked the women of Israel for adorning themselves with moonlets.[12] Jeremiah referred to the worship of the "queen of heaven," [13] this term probably referring to the moon. Job mentioned kissing the hand on seeing the moon,[14] evidently a form of worship which was forbidden to the Israelites.

Postulating as an indisputable fact the doctrine that the sun and moon exert decisive influences on all terrestrial beings and things, it was only a short step for early man to extend the same philosophy to the planets and other stars and, by analogy, to perfect a complete system of astrology that brought the heavenly bodies into complete accord with all earthly occurrences.

THE DOCTRINE AND SCOPE OF ASTROLOGY

Astrology permeated every human pursuit. An inquiry into the stars was made before every venture, whether business enterprise, journey or war. In case of disease or other mishap, the signs of the stars were consulted as to the outcome of the particular misfortune.

9. Psalms **121**:6.
10. II Chronicles **33**:3.
11. II Chronicles **23**:4-5.
12. Isaiah **3**:18.
13. Jeremiah (*a*) **7**:18; (*b*) **10**:2. "Be not dismayed at the signs of heaven."
14. Job **31**:23 and 27.

The astrologic system consisted of two groups of stars. The first group was composed of single and moving stars named planets (Greek: "wanderers"). They were named by the Greeks as follows: Mercury, Venus, earth, Mars, Jupiter, Saturn, sun and moon.

The other group of stars were known as constellations ("stars together"). The members of this group were fixed, usually appearing in clusters. There were sixty-four toward the south of the heaven and twenty-eight toward the north. The latter two groups were separated by a circle of twelve clusters, the zodiac (Greek: "circle of animals"), corresponding to the twelve months of the year. The name of each cluster was based on a supposed or fancied resemblance to an animal or object. The names of the divisions of the zodiac are: Aries, the ram; Taurus, the bull; Gemini, the twin; Cancer, the crab; Leo, the lion; Virgo, the virgin; Libra, the balance; Scorpio, the scorpion; Sagittarius, the archer; Capricornus, the goat; Aquarius, the water carrier, and Pisces, the fishes.

The plan of casting a horoscope is a Greek contribution to astrology to which later ages made but few additions. A brief description of the horoscope will enable one to understand how the art of medicine became the profession of the astrologer.

The horoscope is a circular diagram of the sky divided into twelve meridians. The spaces between the meridians are called diagrams of heaven (*thema caeli*), or houses of heaven (*angeli*). Each house is ruled by a star as it passes from meridian to meridian during its twenty-four hour course. The first house of heaven, which lies in the east 5 degrees above the horizon, signifies life, and the star that passes the house is termed the ascendant (rising star) because it occupies the eastern part of the heaven. The second house symbolizes fortune or riches; the third, fraternity; the fourth, relationship; the fifth, children; the sixth, health; the seventh, marriage; the eighth, death; the ninth, religion; the tenth, dignity; the eleventh, friendship, and the twelfth, animosity or captivity.

In addition to the plan of the houses of heaven and the zodiac, the Greek astrologers brought other signs into play. According to Ptolemy, the sun symbolizes gold; the moon, silver; Jupiter, tin or electrum; Mars, iron; Venus, copper; Saturn, lead, and Mercury, quicksilver. Mercury was associated with quicksilver because of his volatile fickle character. To this day the word mercury is used for quicksilver, and the term mercurial is employed for fickleness. The planets also represent colors. Jupiter symbolizes white; Saturn, green; Venus, yellow; Mars, red, and Mercury mixed colors. The planets also became related to trees, herbs and minerals and animal organs. Indeed, the microcosm was completely dominated by the macrocosm.

Mercury (Fortuna major), Jupiter and Venus (Fortuna minor) were designated good planets. Saturn (Infortuna major) and Mars (Infortuna minor) were considered malignant. The sun, moon and Mars possessed mixed attributes.

Some planets ruled during the day; others, during the night. Jupiter and the sun were day planets; the moon, Mars and Venus occupied their positions at night. Mercury held sway both day and night. The planets represented both sexes. The sun, Jupiter and Mars were masculine, and the moon and Venus were feminine.

The seven planets each ruled one day of the week; hence their names were used to designate the various days of the week: Sunday was named after the sun; Monday, after the moon; Tuesday, after Tiv, the god of war corresponding to the planet Mars; Wednesday, after Wodin, the Germanic equivalent for Mercury; Thursday, after Thor, corresponding to Jupiter; Friday after Frigga, the goddess of love equivalent to Venus and Saturday, after Saturn.

THE HOROSCOPE AS A DIAGNOSTIC INSTRUMENT

A horoscope was cast in the following manner: Having ascertained the exact time of birth of the person being studied, the astrologer traced the star that passed the diagram of the house of heaven at that particular hour. For example, if at the time of birth or conception Jupiter was in the second house of heaven, remembering that Jupiter stands astrologically for fortune, male sex, white and electrum, the astrologic prediction for the child to be born would be as follows: a blond male child who will become a successful jeweler or tinsmith.

In Rome, astrology was introduced by the Greeks at about the beginning of the present era; it became known after the original founders as the "Chaldean art." The Roman Emperor Tiberius was a master in the art of casting horoscopes. He regulated all his actions according to astrologic calculations. The schools of Rome cultivated a complete system of Chaldeo-Greek art. All public and private enterprises were executed in accordance with the signs of the constellations.

THE PLANETS IN THE SACRED LITERATURE

The Old Testament, with its anthropomorphic conceptions of the universe, pictures God as the "Lord of Hosts" and the stars as the "host of heaven." God by His supreme will made the sun and moon stand still.[15] The stars are described as able to "walk" and to "fight" from their courses like warriors."[3] The Pentateuch furnishes little information as to what the ancient Hebrews knew about the "Chaldean wisdom." Isaiah referred to the astrologers as "the stargazers and those

15. Joshua **10**:12.

that prognosticate the months." [16] Jeremiah condemned the astrologers, saying: "Thus saith the Lord: Learn not the way of the heathen and be not dismayed at the signs of the heaven, for the heathen are dismayed at them." [17] Daniel, who was a native of Babylonia, mentioned the *ashaphim* and *gezrin,*[18] which are rendered "the astrologers and the casters of the horoscope," respectively.

Zachariah appears to have hinted at the seven planets when he referred to the "seven eyes of God." [19] He alluded to the sun and the moon as the "eyes of God." A number of stars are also mentioned in the Old Testament, such as: Ksil (Orion), Kimah (identical with Sirius or Pleiades), Ash (hades), Mazoros and Helel (morning star). But beyond referring to their names, nothing else is said about them. In the cuneiform literature, Saturn is spoken of as "the eye of Anu, the lord of the heavens."

The Hebrews believed in the veracity of astrology, although they disapproved of its practice. After the Babylonian exile the names of the seven planets were known to the Hebrews. They are recorded in Talmudic literature as follows: Hama (sun), Lebanah (moon), Zedek (Jupiter), Nogah (Venus), Shabtai (Saturn), Kokab (Mercury) and Maadim (Mars). The Hebrews, being monotheistic, associated the stars with angels and not with divinities. Thus, in the Book of Enoch [20] and the Book of Jubilees the names of seven celestial angels are recorded: Shamshiel (sun angel), Sahariel (moon angel), Rakiel (angel of the sky), Kokebiel (angel of the star), Shehakiel (angel of heaven), Arkiel (angel of the earth) and Barakiel (angel of lightning).

While it is likely that the truth of astrologic forecasts at the beginning of the present era was not questioned by the Hebrews of Palestine, the practice of astrology was not approved of. Josephus censured the Jews for ignoring the visible signs and the indications predicting the destruction of the temple.[21] On the other hand, the Sibylline books praise the Jews because they did not countenance the prophecies of the fortune tellers, magicians or conjurers or practice astrology or seek the oracles of the Chaldeans in the stars.

The sidereal art, however, was popular among the Jews of Babylon of the third and fourth centuries. It was known by several names: *Chaldee, astrologus,*[22] and *itztagnin.*[23] One Talmudic teacher stated:

16. Isaiah **47**:13.

17. Jeremiah.[13b]

18. Daniel **2**:27.

19. Zachariah **4**:10.

20. Enoch **8**:3.

21. Josephus, F.: The Jewish Antiquities, translated into English by W. Whiston, Boston, S. Walker, 1833, book 6, chap. 5.

22. Talmud: Pesahim 113b.

23. Talmud: Sotah 12b; Shabbath 56a.

"The one who can calculate the time of nativities and does not do so, to him is applied the verse, 'the working of the Lord he does not observe.'" [24] Another one, Rabba, said: "Duration of life, progeny, and subsistence depend on the constellations." [25] Rabbi Hanina was of the opinion that "man's wisdom and wealth are according to his nativity and destiny." "Israel is dependent upon nativity." [26] "Even the holy law in the ark is dependent upon the stars." The setting of one's star is a sign that death is near." [27] According to Talmudic legend, Abraham .bore on his breast a large astrologic tablet, in which the fate of every man could be read.[28] Another legend has it that Joab refused to join the conspiracy of Absalom because he had seen the star of David.[29] According to the Talmud, plants also depend on destiny, and even blades of grass have their own particular stars that make them grow.[30]

These beliefs, however, are contradicted by other Talmudic teachers. Said Rabbi Jose of Huzai: "We are not permitted to appeal to the Chaldee, for it is written 'thou shalt be perfect with the Lord, thy God.'" [22] Another Talmudic teacher, Rabbi Yohanan (third century), declared that the planets are not for Israel but only for the nations which recognize the validity of astrology.[26] His colleague, Rab, agreed with this dictum. A legend states that when the Lord told Abraham to go out of his native country he also told him to cease astrologic speculations because there is no nativity for Israel. The noted astronomer and physician, Samuel of Babylon, was an adept astrologist. Although he believed in its reality, he maintained that Israel is not subject to nativity.[31]

The belief in astrology among the early Christians is evident from Matthew.[32] "Herod," stated Matthew, "privily called the Wise men and learned of them exactly what time the star appeared." The Church Fathers, however, were not in accord as to the validity of the stars as a factor in human life. Some of them argued against the doctrines while others accepted them in modified form. Although the Church several times condemned the system, many zealous churchmen cultivated it. Cardinal D'Ailly, of France, is said to have calculated the horoscope of Jesus. He also maintained that the deluge might have been predicted by astrologers.

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24. Talmud: Shabbath 75a.
25. Talmud: Mold Kaltan 28a.
26. Talmud: Shabbath 156a.
27. Talmud: Berohath 55b.
28. Talmud: Babe Bathra 16b.
29. Talmud: Sanhedrin 49a.
30. Talmud: Genesis Rabba **10**:6.
31. Deuteronomy **8**:6.
32. Matthew **2**:7.

The Arabs accepted the "Chaldean wisdom" part and parcel and have made additions to it. Their implicit faith in the influence of the stars was largely responsible for their doctrine of predestination and their fatalism, for they were of the opinion that nothing could alter the fate of a person since it was sealed before birth.

HEALING THROUGH THE STARS

Sidereal medicine reigned supreme well into the eighteenth century. Astrodiagnosis and astrologic remedies were held in high respect, being utilized by physicians and by schools and institutions of healing. Medical astrology had the support of leading physicians throughout the ages. Indeed, astrologists claim that Hippocrates designed the "grand zodiacal man" which appears at present in various astrologic almanacs. They point out that Paracelsus expressed himself strongly in favor of sidereal healing, when he declared: "A physician without the knowledge of the stars can neither understand the cause of, nor cure any disease, not even so much as a toothache."

The inference may be drawn from the Kouyunjik (Nineveh) medical texts at the British Museum that astrologic medicine was originally limited to the prognosis of disease. Some of the texts read as follows:

1. Text 269.—If an eclipse of the sun occurs on the twenty-ninth day of the month of Iyyar, there will be many deaths on the first day.

2. Text 271.—If an eclipse takes place during the morning watch, and lasts throughout the watch, while the wind blows from the north, the sick in Akkad will recover.

3. Text 69a.—If the wind comes from the west upon the appearance of the moon, disease will prevail during this month.

4. Text 207.—If Venus approaches the constellation of Cancer, obedience and prosperity will be in the land . . . the sick of the land will recover. Pregnant women will carry their confinements to a favorable termination.

5. Text 79.—If a halo surrounds the moon and if Regulus stands within, women will bear male children.

6. Text 173.—If Mercury rises on the fifteenth day of the month, there will be many deaths. If the constellation of Cancer becomes obscured, a fatal demon will possess the land and many deaths will occur.

The diagnosis, treatment and complications of disease later became related to the sidereal system of medicine. All parts of the body were brought into direct relation with the stars. Thus Hermes Trismegistus, the previously mentioned author of four volumes on astrology and horoscopy, stated that the special senses and flow of the blood are under the control of the seven planets: "The sun rules the right eye; the moon, the left eye; Saturn controls hearing; Jupiter governs the brain; Venus regulates the senses of taste and smell; Mercury reigns over the tongue, gullet and the organs of speech; and Mars rules over the blood."

Sidereal medicine particularly thrived during the Middle Ages. Marsilus Ficinus (1433 to 1499) in his book on life presented a detailed account of the relationship existing between the organs of the body and the planets. He divided the control of the structure and function of the body among the seven planets, each one being capable of promoting or impeding the growth of the portion of the body it governed, from the time of conception to the last moment of life. Each planet contributed to health or disease, depending largely on how it was placed on the birth chart. Favorable aspects of the planet tended to produce good health. Unfavorable aspects tended to produce morbidity of the body (such as amaurosis, paralysis and ague) and abnormal conditions of the mind (such as irritability, depression, fear, anger, malice and violence).

A recent medical astrologer in an article entitled, "Health and Your Horoscope" [33] gave a general survey of the planets as indicators of health and disease, as follows:

Sun.—Governs the hereditary tendencies, chronic or deep-rooted causes of ill-health, the general vitality of the body. Its dynamic force may lead to various excesses causing a drain on the energies. It represents vitality or prana, the universal life-substance, on which all draw according to the nature of the individual horoscope. It rules the heart, arteries, spinal column, the right eye in a man and the left in a woman and inclines to ailments attacking the constitution, the heart, arteries, spine, and spleen. Excess of solar energy can produce fevers of inflammatory disease, whereas lack of it inclines to anemia, or chronic derangements.

Moon.—Governs the functional workings of the body, diet and emotional tendencies. Moods, emotions, subconscious impressions, apathies and antipathies usually arise according to the Moon's influence. It rules the left eye with a man and the right with a woman. The brain-minded comes under the rulership of the Moon. Its diseases are disorders of the mucous membranes, dropsy, tumors, abscesses, stomach ailments, female disorders or periodic complaints in women, and brain troubles or insanity.

Mercury.—Rules the nervous system, reflexes, sense perceptions, hearing, sight, respiration, and feeling. It inclines to nervous disorders, neurasthenia, ailments arising from worry, indecision, restlessness or over-excitement, etc.

Venus.—Rules the kidneys, throat, and internal reproductive system and gives rise to such diseases as tonsillitis, diphtheria; venereal, kidney, goitre and lymphatic disorders. It strongly affects the emotional nature.

Mars.—The action of this planet is inflammatory due to its excess of vigor of animal vitality. It often indicates effusion of blood, hemorrhage, and health conditions arising through accidents and operations. All infectious and contagious diseases, wounds, muscular and genital disorders come under Mars. Excitement, or violent emotional outbursts are usually due to Mars. It rules the external generative organs, excretory organs, red blood corpuscles and the production of energy.

Jupiter.—Governs the liver, nutrition of the cells, blood and flesh building. Its diseases usually are liver and blood disorders, pleurisy, high blood pressure,

33. Hughes, R. A.: Health and Your Horoscope, Astrologic Guides, May and June 1940, p. 18.

diabetes, fatty degeneration, or all illness that arises from surfeit, congestion and overrichness of the system. Unimpeded assimilation leads to trouble through strong appetities that over-load the system and tax the liver and blood system unduly. Moderation should be the keynote of this planet.

Saturn.—The direct opposite of Jupiter. Jupiter symbolizes expansion while Saturn is the principle of contraction. What Jupiter promises Saturn denies. It affects the human system through obstructions, impediments, cold and sluggishness. This principle, according to the nature of Saturn in the individual horoscope, may impede the blood circulation or the elimination processes resulting in cold diseases, rheumatism or associated diseases. Fear and depression often affect the patient and the Saturn individual creating an attitude that makes real health difficult to maintain.

CASTING OF A MEDICAL HOROSCOPE

The casting of a medical horoscope required, in addition to making annotations of the heavenly bodies at the time of birth, a careful record of the stars at the hour the disease had its onset, for a sidereal physician based his diagnosis, treatment and prognosis on such information. Wise persons, therefore, were in the habit of marking down the exact time when an ailment began. If the disease set in insidiously, the next best precaution was to notice the earliest time when the first symptom appeared. Such observations were considered vital to the welfare of the patient. Observation of the conjunction of the stars was sufficient to indicate which organ of the patient was endangered by the heavenly bodies. If, for example, a person complained of headache, and if the planet presiding over the eye presented an unusual appearance, the eye was naturally considered responsible for the headache and the diagnosis at hand.

The moon, and the sun particularly, played an important part in astrology. The personality and temperament of man, his functional condition and the acute diseases to which he is subject were largely governed by the moon. Hereditary tendencies and chronic derangements depend on the sun. According to Pliny, all acute diseases of the eye in man and beast increase and decrease with the moon, whereas all chronic maladies are influenced by the sun.

It is evident that the astrologic healer was not obliged to see his patient to diagnose the condition and prescribe the proper remedy. All he needed was a graph of the zodiac and a knowledge of the planet in conjunction when the patient was born and when he took sick.

THE ZODIAC AS A MEDICAL GUIDE

The graph of the zodiac, which was the principal diagnostic instrument in the astrophysician's medicine bag, consisted of the twelve signs arranged in a circle and the figure of a man, "the grand man," in the center (fig. 5). Lines drawn from each sign of the zodiac indicate the

part of the body governed by that sign. In case of disease, each sign, from Aries to Pisces, points to the weak or vulnerable part of the body, in the following manner:

Aries.—Diseases of the eyes, head and stomach; also paralysis.

Leo.—Lungs, heart, back and kidneys; also violent, continued fevers.

Saggitarius.—Rheumatism, weakness of the lungs and stomach trouble.

Gemini.—Throat, stomach, nervous disease, worms and eczema.

Libra.—Diseases like nervous prostration and unusual stomach conditions, such as those brought about by excessive worry and impatience.

Aquarius.—Brain trouble, poor circulation and pain in the muscles, head and feet, with an unfavorable prognosis.

Taurus.—Morbid mental conditions, heart trouble, dropsy, tumors, apoplexy and brain disorders.

Virgo.—Certain nervous conditions and stomach troubles; also special reference to carelessness and neglectfulness.

Capricorn.—Indigestion and melancholia as a result of overwork, overambition, or poor judgment.

Cancer.—Weak digestion and gastric troubles.

Scorpio.—Lumbago, gout and weakness of the back.

Pisces.—Pain in the feet, back, head and digestive organs.

The males under the sign of Pisces often suffered periods of despondency and self censure, whereas the females were troubled with fits, melancholia and weeping caused by uterine difficulties.

In this way all bodily diseases were connected with the signs of the zodiac.

TREATMENT AND CHOICE OF HEALER DICTATED BY THE STARS

The sidereal physician was also guided by the heavenly bodies with regards to herbs, roots, barks, berries, plants, drugs and other agents used in the treatment of disease, for all earthly matters, inorganic as well as organic, were under the influence of the planets. Certain planets were thought to govern metals; others, minerals; still others, plants and herbs. If, therefore, the dominant planet at the beginning of a disease was known, it was not difficult to ascertain the proper remedy to prescribe. For example, if the dominant planet at the beginning of the illness was Mercury, a compound of metallic mercury was administered by the astrophysician; likewise, if the controlling planet was Mars (signifying iron), an iron compound was administered.

From the aforementioned account it is evident that the astrologic physician had no choice in the selection of remedies. He was obliged to prescribe the drug or herb indicated by the particular star. The

only time such an extreme position was not maintained was when the substances governed by the planet was not at hand; then the healer was allowed to prescribe a similar substance.

Since all practitioners of sidereal medicine had to do was to observe the dominating star at the time the sickness began, it is apparent that all persons who became ill at the same time under the same star received the same treatment, irrespective of their disease. For example, a patient with a stye would receive the same treatment as a person with epilepsy.

Fig. 5.—A reproduction from a sixteenth century work of G. Bartish (Augendienst, Dresden, M. Stöckel, 1583), showing the connections of all parts of the body to the zodiac. Gemini, who governs the function of the eye, points to the most vulnerable place of the eye. (From Magnus, H.: Superstition in Medicine, New York, Funk & Wagnalls Company, 1905.)

Even the choice of the healer was dictated by the stars, and the patient or his family was not consulted as to the selection. The horoscope dictated who the medical adviser should be. Ptolemy gave special directions under what conditions of the stars the appointment or change of physicians should take place.

The important role astrology played in medicine is evident from the symbol ℞, still used by the modern physician in writing a prescription. This symbol, contrary to the general belief, does not mean recipe. It is the symbol of Jupiter and historically was employed as an invocation of the healing power of the great planetary patron, the healing God, Jupiter. Jupiter-Ammon, Deva-Pitar and Dio-Pitar are some of the names given by the ancients to Jupiter. Thus it is seen that Jupiter, at least in the symbolic sense, still exerts an influence over modern medicine.

STARS GOVERNING INTRAUTERINE LIFE

Since it was of paramount importance to note the name and position of the planet at the time of birth, special care was taken by fathers to engage an astrophysician to be present during parturition, not to assist in the birth of the child but to note the position of the heavenly bodies. The presence of the physician was also necessary in cases in which the newborn infant was troubled with congenital defects or was overtaken by disease soon after birth. According to Jacobus Forliviensis, each planet was in control of one month of pregnancy. If during any period of intrauterine life the embryo was in an unfortunate conjunction, it was bound to suffer. In the prenatal state the organs affected depended on the planet in ascendancy during the particular month of pregnancy that the malevolent conjunction occurred. If a postnatal pathologic condition occurred, the star in conjunction at birth was dominant. Thus if the planets which governed the life of the embryo of the newborn infant were known, proper remedies could be administered for the congenital defects.

Even after the future man passed the day of birth successfully, it did not give him immunity from disease and mishap. Ophthalmia (ophthalmia neonatorum) or morbus Veneris (Venus' disease) frequently attacked the newborn infant and inflicted him with blindness. In such cases the unfavorable conjunction of Venus and the ominous relation of the moon with the signs of the zodiac had to be ascertained.

ASTROLOGY AS VIEWED BY HIPPOCRATES AND GALEN

In Greece, sidereal medicine far surpassed the limits attained in Babylonia. No less an authority than Hippocrates accepted some of its doctrines. In the "Corpus Hippocraticum," passages are found which show more than a passing interest in the astrologic art of healing. "Attention," said the father of rational medicine, "must be paid to the rising of the stars, especially to those of Sirius and Arcturus, and further, to the setting of the Pleiades, for most diseases reach a crisis during such periods." Hippocrates also stated: "He who knows how the change of seasons and the rising and setting of the stars take place will also be able to foresee how the year is going to be. If any one

should be of the opinion that the question belongs solely to the realm of astronomy, he will change his opinion as he learns that astronomy is not of slight but of essential importance in medical art."

Galen accepted some astrologic principles in order to explain his theory of crises. "Contemplate," said Galen, "the critical days, in the course of the moon, in the angles of a geometric figure of sixteen sides; if you find these angles in a favorable constellation, the patient will fare well; badly, however, if evil signs prevail." According to Galen, the critical days are the seventh, fourteenth, twentieth and twenty-seventh. Galen calculated days, weeks and months in accordance with the course of the moon, and in such a manner that the week contained six days and seventeen and a half hours and the month only twenty-seven days and twenty-two hours.

There were also critical years (*anni climacteric*), dangerous to health and life, in which the body was supposed to undergo a thorough change.

SURGERY DICTATED BY THE STARS

Surgery was thought to be particularly benefited by astrologic knowledge. According to Claudius Ptolemy, a scalpel cannot be used on the left eye which is governed by the moon. In his "Centiloquy" he stated: "Pierce not with iron that part of the body which may be governed by the sign actually occupied by the moon." The presence of the moon in the sign governing the part of the body on which the operation was to be made signified danger. According to the Talmud, the new moon is unfavorable for venesection, as is the third day of the month and the day preceding festivals. The most proper time for phlebotomy is the first quarter of the month following the new moon. Mothers in Eastern Europe are still careful to administer vermifuges to their children during that period. During the Middle Ages, English mothers treated styes in children by taking a hair from the tail of a tom cat and applying it nine times to the sick eye of the child during the first night following the new moon.

According to astrologic calculations, Tuesday and Wednesday are good days for blood letting, because on these days, Mars and Mercury, the planets controlling the blood, hold sway. Up to recent years auspicious days for blood letting were proclaimed by astrologists of Baghdad. On these days barber shops were literally flooded with blood.

ASTROLOGY IN THE MIDDLE AGES

Among the Jewish astrologers of the Middle Ages was Abraham Ibn Ezra, philosopher and Bible commentator, who thought astrology to be a sublime science. He frequently referred to it in his commentary on the Bible. He termed the heaven with its constellations "a book of

life [34] in which the destiny of man is written." [35] Ibn Ezra wrote a number of works on astrology and is the author of a horoscope.[36] He referred to Jacob Ibn Tarik, who in the year 777 brought the astrologic tablets of Almansur from India to Baghdad.[37] Mashalla, the court astrologer of Almansur (about 800 A. D.), gained reknown for two books on astrology, "Eclipse" and "Questions." Both of them were

Fig. 6.—A fifteenth century drawing indicating the parts of the body from which blood is to be drawn in various diseases, as indicated by the zodiac. The place of venesection in cases of headache and ocular pain is indicated by *1*, and the spot where blood is to be drawn in diseases of the eye, by *3*. (From Magnus, H.: Superstition in Medicine, New York, Funk & Wagnalls Company, 1905.)

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34. Ibn Ezra: Commentary on Daniel **11**:29.

35. Ibn Ezra: Commentary on Genesis **19**:9; Commentary on Exodus **6**:3-33.

36. Ibn Ezra: A Letter to the Men of Marseilles, Steinschneider Catalogue, Bodleian Library, Hebrew Collection, pp. 136-150.

37. Astrology, in Jewish Encyclopedia, New York, Funk & Wagnalls Company, 1902, vol. 2, p. 241.

translated by Ibn Ezra into Hebrew. Astrology was made the basis of Messianic calculations by numerous medieval rabbis.

Maimonides, the celebrated physician of Cordova, opposed astrology in any shape or form. He cited biblical authority to prohibit sidereal practice: "Ye shall not observe times." "Astrology," said Maimonides, "is a disease, not a science; a tree under the shadow of which all sorts of superstition thrives, and which must be uprooted in order to give way to the tree of knowledge and the tree of life.[38]

In the thirteenth century, Emperor Frederick the Second greatly encouraged the practice of astrology in all its phases. This monarch was so positive of the virtue of astrologic doctrines that he did not decide on any state enterprise until he first consulted the stars regarding his political fortunes. His reign was marked by all sorts of occult beliefs. After his death, two talented physicians entered the astrologic field. One was Arnold of Villanova (1235-1312) and the other was Petrus Aponeses (1250-1315). From that time on until the seventeenth century, representatives of all professions devoted themselves to the doctrine of the heavenly bodies.

Astrology was particularly popular in Germany. Albrecht of Prussia subscribed to astrologic medicine. Thomas Erastus, another well known physician, was not permitted to begin a course of treatment on the ruling Count of Henneberg until he had consulted the stars.

Paracelsus ascribed more medical virtue to the stars than to the humoral theory. He gave instances of insane persons who were deprived of their wits by motions of the moon. He believed that the ascendant star was the true cause of disease. He was of the opinion that all parts of the body stand in direct relation to the stars. The seven great organs, the brain, heart, lungs, gall, liver, kidneys and spleen, correspond to the moon, sun, Mercury, Mars, Jupiter, Venus and Saturn, respectively. He classified seven kinds of pulses corresponding to the seven plants.[39]

Among those who adhered to the superstition of astrology were Tycho de Brahe, Cardan, Robert Burton and the eminent physicist and astronomer Keppler (1570-1630). Keppler is said to have received huge fees for his professional astrologic advice. One time he drew a prediction from a comet which came true. He corroborated the prediction of Tycho de Brahe that in the north of Finland a prince would be born who would lay Germany in waste and die in 1632. This, as it happened, came true. Gustavus Adolphus was born in Finland, overran Germany and died in 1632. Keppler spoke of astronomy as "the wise

38. Maimonides: A Letter to the Men of Marseilles, Steinschneider Catalogue, Bodleian Library, Hebrew Collection, 1903, p. 931.

39. Cited by Magnus, H.: Superstition in Medicine, authorized translation from the German, edited by J. L. Salinger, New York, Funk & Wagnalls Company, 1905, pp. 137-138.

mother" and of astrology as "the foolish daughter," but he remarked that the existence of the daughter was necessary to the life of the mother. Even Francis Bacon, who abused the astrologers and alchemists of his day, believed in the veracity of astrology.

Stoffer, a German astrologist, predicted that in 1524 three planets would meet in the aqueous sign of Pisces. He therefore prophesied a universal deluge for that year. President Auriel, of Toulous, on hearing this prophecy, promptly built for himself an ark in order to escape the deluge; the flood, however, turned out to be a drought.

Robert Burton, famous author of "The Anatomy of Melancholy," many years before he died predicted from the horoscope the year of his own death. He died on Jan. 25, 1640.

It was a common practice for men to conceal the day and year of their birth until they found a competent astrologer. Cardan stated that Martin Luther changed his birthday in order to avoid an unfortunate horoscope.

Astrologers did not always have easy sailing. They were often dominated by terror and occasionally endured martyrdom when their predictions were either too true or too false.

The discovery by Copernicus (1473-1543) that the sun is the center of planetary space and that the diurnal turning of the earth on its axis accounts for the apparent revolution of the stars has broken down the very foundation of astrology among cultured men. It ceased to have any scientific pretense, and therefore little credence is given by cultured men of Western Europe and America to sidereal medicine. It is looked on as a form of witchcraft, and its practice is limited to fortune tellers. Traces of this belief, however, are still preserved in every vernacular. In the English language, terms such as "disaster" for "ill luck," "consider" or "contemplate" for "observe," "jovial" (Jupiter) for "merry," "saturnine" (Saturn) for "gloomy" and "lunatic" (moon struck) for "insane" are numerous. In many languages the word for cataract is "star"; it is possible that it refers not only to its likeness to a star but to some ancient astrologic doctrine. Expressions such as "born under a lucky star" or "an evil star" are in common use. English classical poetry abounds with astrologic expressions such as "there, an ill planet reigns. I must be patient until the heavens look with an aspect favorable." "Our jovial star reigned at his birth" (Shakespeare). "I will look on the stars and look at thee; and read the passage of thy destiny" (L. E. Landon).

In spite of the scientific evidence against astrology, it is difficult to eradicate it. The large number of astrologic journals still published here and abroad furnish ample evidence that astrology is by no means dead. The fact that there has always been and always will be a desire

of credulous and ignorant persons to look into the future encouraged numerous charlatans to continue using the label of astrology for selfish purposes.

SUMMARY AND CONCLUSIONS

For ages, sidereal medicine was an oppresive nightmare to the sick and disabled. It buried the art and science of medicine under an avalanche of false ideas and delusions.

The physician, instead of studying the patient for the purpose of diagnosis and treatment, studied the signs of the stars. It was not even necessary to see the patient to diagnose the disease, as therapy was not directed at the disease but to the signs of the stars. If the patient was born under a certain unlucky star, he was bound to suffer; there was no way to prevent it, and there was no use trying. Furthermore, all persons who were born under the same star received the same medical treatment, regardless of the particular illness.

The stars gave the healer information as to when the disease would begin, how long it would last, what organs would be affected and whether the patient would recover completely or die. If the stars prognosticated death, there was no use prescribing medicine; but if recovery was indicated, the stars pointed to the kind of medicine to be used.

The widespread medical superstition was condemned by Maimonides. "Fools," he wrote, "have composed thousands of books vain and vacuous, . . . It is a fatal mischief that whatever is found in books is instantly accepted as truth, especially if the books are ancient." [40] Elsewhere he stated: "Regard not all that you see in books as convincing proof. The liar lies with his pen as readily as with his tongue." [41]

40. Maimonides: Responsa **2**:25a.
41. Maimonides: Iggereth Temon **2**:5.

EXPERIMENTAL STUDIES OF OCULAR TUBERCULOSIS

VI. THE EFFECT OF SENSITIVITY AND IMMUNITY ON THE EXPERIMENTAL LESIONS OF OCULAR TUBERCULOSIS

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In the study of the relation of ocular sensitivity, ocular activity and cutaneous sensitivity in immune-allergic rabbits,[1] it was noted first that both the course of the ocular tuberculosis and the further development of ocular sensitivity after inoculation of the eyes were restrained in comparison with their development in the normal rabbit after similar inoculation. It was further noted that in the early stages of the ocular tuberculosis in immune-allergic rabbits the ocular activity and ocular sensitivity paralleled each other, but that in the later stages of healing and repair there was a definite lag in the subsidence of the ocular sensitivity after apparent healing of the eyes. This brought up the question that factors other than the subsidence of ocular sensitivity might influence the healing of the local process in the eyes. To study further the influence of general immunity, local sensitivity and possibly local immunity on the course and character of the ocular lesion, the studies here reported were undertaken.

EXPERIMENT 1: INFLUENCE OF SYSTEMIC IMMUNITY ON THE PREVENTION AND COURSE OF SECONDARY OCULAR TUBERCULOSIS

When immune-allergic rabbits were first inoculated in the eyes with the dose of tubercle bacilli which produced a progressive and caseating tuberculosis in the eyes of normal rabbits, it was found that the immunity present from the previous systemic infection was sufficient to prevent the growth of the bacilli and the development of any local tuberculosis. A dose approximately fifty times as large was found to be the minimum

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1. Woods, A. C.; Burky, E. L., and Friedenwald, J. S.: Experimental Studies of Ocular Tuberculosis: IV. The Relation of Ocular Sensitivity, Cutaneous Sensitivity and Ocular Activity in the Immune-Allergic Rabbit, Arch. Ophth. **23**: 351 (Feb.) 1940.

amount which produced a satisfactory ocular tuberculosis, and even with this dose the resulting inflammation was usually marked by an absence of caseation and necrosis.

The following experiment was undertaken to determine to what extent the immunity existing at the time of inoculation could inhibit the growth of the tubercle bacilli in the eye and determine the course of the subsequent tuberculous inflammation.

Plan of Experiment.—Sixty-five rabbits were systemically inoculated by injection into the groin in the usual manner on July 1, 1937. Three months thereafter, on October 4, their cutaneous sensitivity was determined. On November 2 0.2 cc. of an undiluted and unfiltered six week old culture of bacilli, thoroughly shaken to produce a homogeneous suspension, was injected into the anterior chambers. This was a dose at least several hundred times larger than the minimum dose capable of producing secondary ocular tuberculosis.

Results.—There was a definite ocular reaction to the tuberculin in the inoculum, similar to that observed in other experiments. This reaction began a few hours after inoculation and reached its height in forty-eight hours. Thereafter it did not subside, but there ensued a rapid, destructive, spreading tuberculous infection with marked caseation and necrosis. By December 17, six weeks after the inoculation, the eyes of 12 of these rabbits, or about 20 per cent, had ruptured and the eyes of 8 others showed buphthalmos. This was a higher incidence of advanced caseation than was observed in the normal rabbits inoculated with the dilute paper filtrate suspension. Indeed, the entire tuberculous process was much more severe, and the clinical evidence of ocular sensitivity, manifested by caseation and necrosis, was more marked than in the normal rabbits. Hard tubercles were never observed in these immune-allergic rabbits inoculated with this massive dose of bacilli.

It is evident from this experiment that the ability of the immunity to control the growth and spread of the bacilli in the eye is only relative. If a sufficiently heavy dose of bacilli is introduced into the eye, the immunity is overcome and the ensuing tuberculous inflammation is radically altered. Instead of a slowly progressive, restrained tuberculous process with hard tubercles of the iris developing in 50 per cent of the rabbits, there occurs a violent inflammation, rapidly progressing with caseation and necrosis, in every way comparable with, and even more severe than, the reaction observed in normal rabbits after the inoculation of the eyes with the diluted paper filtrate of the culture.

EXPERIMENT 2: INFLUENCE OF HIGH AND LOW SENSITIVITY ON THE OCULAR LESION

There is considerable individual variation in the degree of cutaneous sensitivity which may follow identical systemic inoculations in normal rabbits. It has already been shown that the ocular sensitivity of such

rabbits parallels the cutaneous sensitivity. This experiment was undertaken to determine if a high or low sensitivity, within the limits observed secondary to the usual systemic inoculation, could influence the type or course of the ocular lesion produced by later inoculation of the eye with the minimum dose of tubercule bacilli capable of producing secondary ocular tuberculosis in the average immune-allergic rabbit.

Plan of Experiment.—Seventy-five rabbits were systemically infected with tubercle bacilli on Jan. 25, 1938. Three months later they were tested for cutaneous sensitivity. Two groups of 12 rabbits each were selected on the basis of their cutaneous sensitivity. One group consisted of rabbits with a cutaneous sensitivity of 2 or more, while the second group consisted of rabbits with a cutaneous sensitivity of 0.5 or less. Since previous experiments [2] have shown that in normal rabbits, systemically infected, the cutaneous and the ocular sensitivity are approximately parallel, it is a fair assumption that the rabbits with high cutaneous sensitivity likewise had high ocular sensitivity and vice versa.

Both groups were then given identical intraocular injections of tubercle bacilli, 0.2 cc. of the undiluted paper filtrate of a six week old broth culture. The development of the ocular tuberculosis and the cutaneous sensitivity to purified protein derivative were then followed as in previous experiments. At two week intervals the ocular sensitivity of 2 rabbits in each group was determined, and the rabbits were killed.

There are therefore available for analysis in this experiment observations on the character and course of the ocular tuberculosis, the ocular sensitivity and the cutaneous sensitivity in rabbits with initial high and low general sensitivity and ocular sensitivity to purified protein derivative.

Results.—The graphs indicating the course of the ocular sensitivity, ocular activity and cutaneous sensitivity of the two series are shown in charts 1 and 2. The rabbits with high cutaneous sensitivity, in which there was presumably a high degree of ocular sensitivity, showed a severe immediate reaction to the inoculum, averaging over 2. This initial reaction subsided to a great extent within two weeks. The eyes then showed a smoldering reaction. The inflammation gradually increased in intensity, hard tubercles of the iris developing in about 50 per cent of the rabbits, while ordinary keratoiritis developed in the remainder. However, no caseation or necrosis was observed in any of the rabbits. Three months after the intraocular injection, when the last rabbits were killed, the eyes still showed an activity of almost 2. During this period of observation the ocular sensitivity was maintained at a high level, a little over 2, and the ocular activity closely paralleled the ocular sensitivity. The cutaneous sensitivity steadily dropped, however, and at the end of the experiment was almost gone.

The animals with the low sensitivity, in which there was presumably a low degree of ocular sensitivity, showed only a slight immediate reac-

2. Woods, A. C.; Burky, E. L., and Friedenwald, J. S.: Experimental Studies of Ocular Tuberculosis: I. Relation of Ocular Sensitivity to Cutaneous Sensitivity in the Systemically Infected Rabbit, Arch. Ophth. **19**:229 (Feb.) 1938.

tion, slightly less than 1. This subsided within a week, and a progressive ocular tuberculosis developed which was comparable with that shown by the rabbits with high cutaneous sensitivity, but of lower intensity. The eyes of the last pair killed three months after the ocular inoculation still showed moderate activity. In these eyes the ocular sensitivity, presumably low at the time of inoculation, had reached a fairly high level at the end of the second week and continued at approximately this same level for the duration of the experiment. Histologic examination of these eyes confirmed the clinical observations.

This experiment indicates that when immune-allergic rabbits are given a moderate amount of inoculum in the eyes, the effect produced by

Chart 1.—Course of ocular activity and of ocular and cutaneous sensitivity in rabbits with initial high cutaneous sensitivity. *A* indicates cutaneous sensitivity; *B*, ocular activity, and *C*, ocular sensitivity.

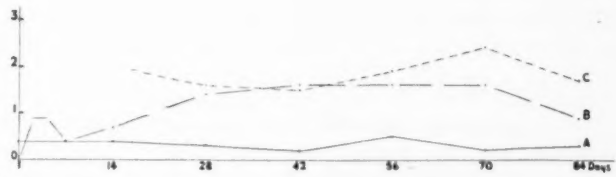

Chart 2.—Course of ocular activity and ocular and cutaneous sensitivity in rabbits with initial low cutaneous sensitivity. *A* indicates cutaneous sensitivity; *B*, ocular activity, and *C*, ocular sensitivity.

an initial high ocular sensitivity is limited. The immediate reaction following inoculation, due almost certainly to the tuberculin in the inoculum, is more intense, and the general picture of the ensuing tuberculosis is more severe. However, the type of the tuberculous reaction is essentially the same as in rabbits with low initial sensitivity, the ocular lesions differing only in degree.

EXPERIMENT 3: EFFECT OF DESENSITIZATION ON THE OCULAR LESION

To study further the influence of sensitivity on the experimental ocular lesion, an experiment was undertaken the aim of which was to compare the ocular lesions and both the ocular and the cutaneous sensi-

tivity of two series of similarly inoculated immune-allergic rabbits, the difference in the two series being that in one series the sensitivity incidental to a previous infection was present while in the second series this sensitivity had been removed by desensitization with tuberculin.

Plan of Experiment.—Forty normal rabbits were inoculated systemically on Jan. 23, 1939. Six weeks later, on March 9, they were tested intracutaneously with purified protein derivative and found to be sensitive. They were then started on tuberculin therapy, 0.1 cc. of pure tuberculin (old tuberculin) being given intracutaneously twice a week. An intracutaneous test with purified protein derivative on April 26 showed that the greater number of animals were becoming insensitive. Injections of tuberculin were continued, and on May 10 all rabbits were tested for cutaneous sensitivity by intracutaneous injection of both purified protein derivative and 0.1 cc. of a six week old culture of living tubercle bacilli. On this same date the right eyes of all 40 rabbits were inoculated with the usual inoculum of tubercle bacilli—0.2 cc. of the undiluted paper filtrate of a six week old culture of virulent human tubercle bacilli.

The rabbits reacted somewhat differently to these cutaneous and ocular inoculations. Some rabbits, still sensitive to tuberculin, showed inflammatory reaction in the eyes and in the skin, due to the tuberculin in the inocula. Others, apparently completely desensitized by the injections of tuberculin, showed neither ocular reactions to the tuberculin in the inocula nor cutaneous reactions to the injection of either purified protein derivative or the living bacilli. Two rabbits showing the highest degree of reaction to the inocula and 2 showing no reactions were killed for histologic examination of the eyes. The eyes of the rabbits showing reaction to the inoculation of tubercle bacilli showed the usual histologic picture of acute inflammation described for similar animals in the previous papers. The eyes of the rabbits showing no reaction to the bacilli were essentially negative histologically.

On the basis of their cutaneous reactions to purified protein derivative and living tubercle bacilli, and the ocular reactions to the inoculation of the bacilli, these 40 rabbits were divided into two groups. The first group, hereafter referred to as group A, consisted of 17 rabbits in which complete desensitization had apparently been achieved. These rabbits showed practically no reaction either to the intracutaneous injection of purified protein derivative or tubercle bacilli or to the intraocular injection of living bacilli suspended in tuberculin. The second group, known hereafter as group A,[1] consisted of 18 rabbits which were not completely desensitized, all showing more or less reaction to the various inoculations, the average cutaneous sensitivity of this group being 0.7 and the average ocular sensitivity being 1.7.

As a further control series, 20 immune-allergic rabbits, known hereafter as group B, were selected. These rabbits had received their systemic inoculation on March 9, 1939. On May 10 their average ocular sensitivity was 2.0 and their average cutaneous sensitivity 2.1. The right eyes of these rabbits were inoculated with the usual dose of tubercle bacilli on May 10.

There are, therefore, available for comparison of the development and course of the ocular tuberculosis three similarly inoculated groups of immune-allergic rabbits, the three groups differing only in their degree of ocular and cutaneous sensitivity at the time of inoculation and in their after-treatment. The rabbits of group A were completely desensitized prior to ocular inoculation. In these rabbits the systemic injections of tuberculin were continued twice weekly with the aim of maintaining this desensitization. The rabbits of group A[1] were only partially

desensitized at the time of the ocular inoculation, and all injections of tuberculin were now discontinued in these rabbits, the sensitivity being allowed to return, would it do so. The rabbits of group B were highly sensitive at the time of inoculation and received no tuberculin at any time to disturb their sensitivity.

The eyes of the rabbits in all these groups were examined at weekly intervals, and the degree of ocular inflammation resulting from the inoculation with tubercle bacilli was plotted on a numerical scale. The cutaneous sensitivity of all rabbits was determined at intervals of three weeks. The ocular sensitivity of specimen pairs from each group was likewise determined at intervals of three weeks, and the tested pairs were killed for histologic examination of the eyes after clinical estimation of the ocular reaction to purified protein derivative had been made.

The period of observation on these rabbits was five and a half months, from May 10 to Nov. 1, 1939.

Course of Cutaneous Sensitivity (chart 3).—The cutaneous sensitivity of the rabbits of group A, which received tuberculin during the entire length of the experiment, remained practically at zero during the first twenty weeks of the experiment. In the last five weeks of the experiment, when the number of surviving animals was only 5 and the average was thus more influenced by individual variations, the cutaneous sensi-

Chart 3.—Development and course of cutaneous sensitivity in rabbits of groups A, A [1] and B.

tivity reached a high of 0.4. Evidently the injections of tuberculin were sufficient to control any cutaneous sensitivity that might have developed or returned.

In the rabbits of group A [1] the cutaneous sensitivity declined slightly during the first few weeks of the experiment, possibly influenced by the recent injections of tuberculin. Thereafter it increased slightly, reaching a high of 1.0 at the end of the twelfth week. It then declined slowly with many fluctuations throughout the duration of the experiment.

In the rabbits of group B the cutaneous sensitivity fluctuated slightly throughout the course of the experiment, the general course being downward, and at the close of the experiment the average cutaneous sensitivity was 1.0 as compared with an initial cutaneous sensitivity of 1.7. In the rabbits of both groups A [1] and B, as in former experiments, the antigenic stimulus from a tuberculous focus within the eye was apparently insufficient to influence the cutaneous sensitivity.

Course of Ocular Sensitivity.—The course of ocular sensitivity of these three groups of rabbits is shown in chart 4. In the rabbits of group A the ocular sensitivity remained at a low level up to the ninth week, the development of the ocular tuberculosis being slow. From

the ninth to the sixteenth week, during which time the ocular activity reached its high level of 1.4, the ocular sensitivity gradually rose. Thereafter it declined slightly but was still present in the animals surviving at the end of the experiment. In this series of rabbits treated with tuberculin the ocular sensitivity at its maximum was only one-half the intensity reached by the eyes of the two groups not treated with tuberculin.

In the rabbits of group A [1] the ocular sensitivity declined slightly during the first few weeks, as did the cutaneous sensitivity. Thereafter as the tuberculosis became disseminated throughout the eye the local sensitivity gradually increased, reaching its maximum of 2.0 at the fifteenth week and declining slightly until the end of the experiment. In the rabbits of group B the ocular sensitivity remained fairly constant for the first fifteen weeks, thereafter declining steadily as the activity waned.

Development and Course of Ocular Activity (Tuberculous Inflammation).—The incubation period for the development of the ocular tuber-

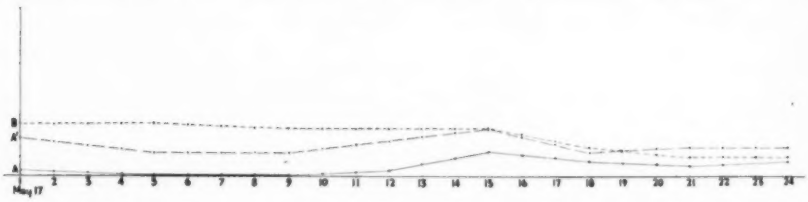

Chart 4.—Development and course of ocular sensitivity in rabbits of groups A, A [1] and B.

culosis was longer and the incidence of immunity to the development of ocular inflammation was greater in the rabbits of group A than in the other two groups. Of the 17 rabbits in group A, 5 did not show any ocular inflammation during their period of observation, this being five, eight, eleven, fourteen and twenty-five weeks, respectively. The incubation period of the 12 rabbits in this group in which ocular tuberculosis did develop varied from three to fourteen weeks, an average of seven weeks. In group A [1] ocular tuberculosis developed in all but 1 rabbit, and the observation period for this animal was fourteen weeks. In the 17 rabbits in which ocular tuberculosis did develop the incubation period varied from three to twelve weeks, the average being four weeks. In group B, 2 rabbits did not show ocular inflammation during observation periods of sixteen and twenty-three weeks, respectively. In 16 rabbits in this group ocular disease developed, the incubation period for all being two weeks.

While the incidence of absolute immunity in the three groups, 5 for group A, 1 for group A[1] and 2 for group B, may not be statistically

significant, the wide difference in the incubation period, seven weeks, four weeks and two weeks, respectively, for the three groups, does appear significant.

The average ocular readings of the reacting rabbits of the three groups are shown in chart 5. Only the rabbits in which ocular tuberculosis actually developed are included in these estimations. The curves are plotted on this basis in order to eliminate the error which would result from longer incubation periods of the rabbits in groups A and A.[1] The curves therefore show a true comparison of the degree of inflammation present in the nonimmune members of the three groups.

The results are evident. For the first four months, during which the ocular inflammation reached its height and finally began to decline, the degree of ocular inflammation was much less in the desensitized group than in either of the control groups. In the last six weeks of the experiment, when the ocular inflammation was declining sharply in all three groups, the curves are almost identical. Further, the initial reception of tubercle bacilli in the eye was attended with a violent inflammatory

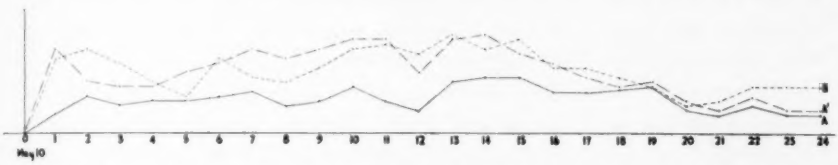

Chart 5.—Average ocular activity of reacting rabbits of groups A, A[1] and B.

reaction in the two sensitive groups and with little reaction in the insensitive group of rabbits.

This experiment shows clearly the influence of sensitivity and insensitivity to tuberculin in the development and course of ocular tuberculosis in the systemically infected rabbit. The sensitive rabbits show an apparently greater susceptibility to infection with the same inoculum, a much more intense reaction to the reception of tubercle bacilli in the eye and a more violent tuberculous disease in the eyes than do the insensitive rabbits.

This experiment also allows some interesting speculation on the action of tuberculin. It is evident that the use of tuberculin prior to the ocular inoculation produced a varying degree of desensitization, almost complete in the rabbits of group A but only partial in the rabbits of group A.[1] The use of tuberculin in the rabbits of group A after inoculation of the eyes may have controlled somewhat the development of ocular sensitivity in this group, for here it never reached the degree attained in the other two groups. This, however, is not clearly demonstrated, for it is known that the degree of sensitivity developing in an infected eye closely parallels the development and intensity of the local infection;

and in the rabbits of group A the local disease was of low degree or did not develop. It may well be that the lack of local sensitivity and the absence of initial inflammatory reaction allowed greater play for the immunity factors and may even have enhanced their action. Certainly, however, it can be said that the desensitization produced by injections of tuberculin has a favorable action on the course and development of ocular tuberculosis.

EXPERIMENT 4: DEVELOPMENT OF LOCAL IMMUNITY

In the first experiments [1] on immune-allergic rabbits it was noted that while in the early stages of the ocular tuberculosis, ocular sensitivity and ocular activity paralleled each other, in the late stages healing and repair might take place while there was still a demonstrable ocular sensitivity, although this later gradually declined. This introduced the question of what factors other than the subsidence of local sensitivity might influence healing. Such factors might obviously be: (*a*) an increase in the general immunity produced by the local tuberculous infection; (*b*) an exhaustion of the general reaction power of the eye and (*c*) the development of a local ocular immunity. These possibilities were investigated in the following manner:

EXPERIMENT 4 a.—Was there an increase in the general immunity produced by the local ocular disease? This appeared unlikely, for it had already been shown in the previous studies of this series that the antigenic stimulus from local ocular tuberculosis is insufficient to influence the cutaneous sensitivity. The following experiment was undertaken to investigate further this first point. The questions were, first, Are eyes which have recently recovered from an attack of tuberculosis more resistant to reinfection and, if so, could this be due to an increase in the general immunity?

Plan of Experiment.—Eight normal rabbits were systemically given injections of living virulent tubercle bacilli into the groin on Jan. 23, 1939. Three months later, on May 1, the right eyes were inoculated with the usual dose of 0.2 cc. of an undiluted paper filtrate of a six week old culture of the same tubercle bacillus. In all the rabbits there developed the usual picture of ocular tuberculosis previously described [1] in immune-allergic animals. This persisted for about three months and then gradually subsided. At the end of six months 7 of the rabbits showed no activity of any kind, the eyes having been entirely quiet for three months. The eighth (no. 446) still showed a faint trace of smoldering activity. The entire group was inoculated in both eyes with 0.2 cc. of an undiluted paper filtrate of a six week old culture of the same bacillus on Oct. 30, 1939. This was a reinoculation of the previously diseased right eye and an initial inoculation of the left eye.

Results.—The results of this experiment are shown in chart 6. The previously diseased right eyes appeared highly sensitive. This was obviously due to the previous ocular disease, for the cutaneous sensitivity was low. These right eyes reacted with an immediate sharp inflamma-

tion to the tuberculin in the inoculum. This reaction gradually subsided, however, and in one month the eyes were practically quiet and throughout the period of observation of ten weeks did not show any further symptoms of tuberculous inflammation. This clearly indicates that these eyes, recently recovered from an attack of local tuberculosis, were at least temporarily resistant to reinoculation with the minimum inoculum capable of producing tuberculosis in the immune-allergic rabbit.

The course in the previously normal left eyes was radically different. The initial reaction to the tuberculin in the inoculum was minimal. This would be expected, for the general sensitivity was low, and a previous experiment had shown that a tuberculous process in one eye does not produce a selective sensitization of the second eye.[3] In these left eyes, however, there gradually developed a typical ocular tuberculosis which ran the usual course of about three months, the eyes not being entirely quiet until the early part of February 1940.

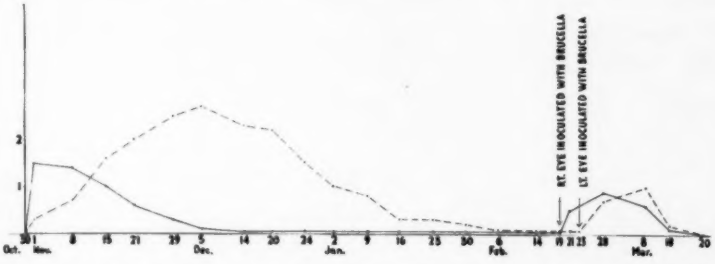

Chart 6.—Inflammatory reaction and tuberculosis activity in right eyes (previously diseased) and left eyes (previously normal) of immune-allergic rabbits. The continuous curve pertains to the right eyes and the broken curve to the left eyes.

It is evident, therefore, that there was no increase in the general immunity produced by the previous tuberculosis of the right eyes, for the disease in the left eyes of these animals was of equal intensity to that observed in other immune-allergic animals which had not had any previous ocular disease.

EXPERIMENT 4 b.—The next question was, Can the nonreactivity of the right eyes to the second injection of tubercle bacilli be due to an exhaustion of their reactive capacity by the previous attack of tuberculosis? This appeared unlikely, for the initial reaction of these eyes to the tuberculin in the inoculum would indicate that their reactive capacity was unimpaired. However, to test this point further the following experiment was undertaken.

3. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis: V. The Question of Organotropism, or the Selective Sensitization of the Second Eye, Arch. Ophth. **23**:363 (Feb.) 1940.

Plan of Experiment.—The same 8 rabbits used in experiment 4a were used again. When the left eyes had completely recovered from the local attack of tuberculosis and the right eyes had been quiet for several months, a living culture of Brucella suis was injected into both the right and the left eyes. The injections were done into the right eyes on February 19 and into the left eyes on February 23.

Results.—The results are shown in chart 6. In both right and left eyes there immediately developed the typical inflammatory reaction seen in moderately severe infections of the eye due to Brucella. The eyes, already scarred and vascularized by the former attack of tuberculosis, showed fresh circumcorneal injection, fresh infiltrates in the cornea and further vascularization. As controls, 10 immune-allergic rabbits without previous ocular disease were similarly inoculated with Brucella. The reactions were more intense in the previously tuberculous eyes than in the controls.

It is clearly evident, therefore, that no loss in the reactive capacity of the tuberculous eyes had been produced by the previous attack of ocular tuberculosis, and the failure to react to further inoculation with tubercle bacilli must be attributed to some other cause.

EXPERIMENT 4 c.—Since the nonreactivity of previously tuberculous eyes to a second injection of tubercle bacilli cannot be attributed either to an increase in the general resistance of the animals or to a loss of reactive capacity of the eyes, it follows by elimination that there must be a local increase in the bacteriostatic action or the specific resistance to tubercle bacilli. This gives a ready and plausible explanation for the healing of these eyes while ocular sensitivity was still present. The nature of this increased local resistance is, however, far from clear. Is it due to the increased vascularization of the eyes produced by the preceding tuberculous inflammation or to an enhanced resistance of the fixed cells of the eye or to a combination of both? Is the increased resistance chiefly humoral or chiefly cellular, or due to a combination of both? It is obvious that if this question can be answered, prolonged investigation will be necessary. However, the following preliminary experiment throws a little light on the question.

Plan of Experiment.—Twenty normal rabbits were inoculated systemically with tubercle bacilli on Dec. 6, 1939. Two months later, on Feb. 5, 1940, the anterior chambers of the right eyes of 10 of these rabbits were inoculated with a living culture of B. suis, and the conjunctival sacs of the remaining 10 were inoculated with a living culture of Listerella monocytogenes, which often produces marked vascularization of the eyes. On March 6, when the resulting disease in both groups had run its course and the eyes were free of active inflammation, 5 rabbits with highly vascularized eyes were selected. Four of these had been infected with Brucella and 1 with Listerella. The usual dose of living tubercle bacilli was then injected into the nonspecifically vascularized eyes of these immune-allergic tuberculous rabbits.

Results.—All 5 rabbits showed an immediate inflammatory reaction to the tuberculin in the inoculum, indicating a fair degree of ocular sensitivity to tuberculin from the preceding systemic infection and likewise a reactive capacity of the eyes. This subsided almost completely within the first week. Thereafter in 3 of the rabbits there gradually developed a mild restrained tuberculous infection in the control eyes, which never averaged over 1.2 on the numerical scale, and within two months the eyes had practically recovered. In the fourth rabbit only a mild iritis developed one month after inoculation with the tubercle bacilli. This lasted only one week and appeared to be an exacerbation of the former infection with Brucella rather than an active tuberculous infection. The fifth rabbit recovered from the initial reaction to tuberculin and did not have any further ocular inflammatory symptoms during the period of observation.

This incidence of immunity, 2 out of 5 rabbits, is not statistically significant, for occasionally in a group of immune-allergic rabbits certain animals are encountered which are resistant to later inoculation of the eyes with tubercle bacilli. However, the immunity of these 2 rabbits, coupled with the low grade and comparatively short duration of the disease in the other 3 rabbits, as compared with the controls, indicates that vascularization of the eyes in immune-allergic rabbits enhances the local immunity of the eyes to reinfection. It by no means excludes the possibility of a local tissue immunity developing in the eyes as a result of the disease. This remains a distinct, though unproved, possibility. Since it is well known that the phagocytosis of tubercle bacilli is chiefly by the macrophages, it is not at all remarkable that an increased blood supply to an infected area should enhance the immunity. The probability is that the local immunity acquired by the eye as a result of a previous infection is, like other immunity reactions in the body, both humoral and cellular. On how long this local immunity may persist, we have no accurate information. In the right eyes of these rabbits it persisted at least three months. These are all points for further investigation.

SUMMARY AND CONCLUSIONS

1. A previous systemic tuberculous infection endows the eyes of such infected animals with a relative immunity to later inoculation with tubercle bacilli. This immunity is only relative, however, and if the dose of injected bacilli is of sufficient size, this immunity may be overcome and a necrotizing, caseating lesion produced similar to that seen in normal animals given injections of a smaller dose.

2. High and low ocular sensitivity, within the limits that may follow a systemic infection, do not materially alter the final picture of a secondary ocular tuberculosis. The rabbits with high sensitivity do show a more violent initial reaction and a higher degree of inflammation

in the early phases of the lesion. However, if the ocular sensitivity is allowed to develop in the rabbits with low sensitivity, the final picture is quite similar.

3. One series of immune-allergic rabbits was completely desensitized by injections of tuberculin and the tuberculin continued throughout the course of the experiment in the effort to maintain the desensitization. A second group of rabbits was partially desensitized, but the tuberculin was then discontinued and their sensitivity allowed to return. A third group was not treated with tuberculin at any time. All three groups were similarly inoculated in the eye with tubercle bacilli. The desensitized group showed a higher incidence of immunity, a longer incubation period in the reacting rabbits and a lower intensity of the ocular tuberculosis than was shown by either of the two sensitive groups.

4. Following an attack of ocular tuberculosis, there develops in the previously diseased eyes of immune-allergic rabbits at least a temporary increased resistance to reinoculation. This increased local resistance is not due to an increase in the general immunity brought about by the local ocular disease nor to an exhaustion of the reaction-capacity of the eyes. The indications are that the increased vascularity of the eyes produced by the former tuberculosis plays a part in the increased local resistance state. It is also probable there may be a local tissue immunity produced by the former disease.

BIRTH INJURY OF THE CORNEA WITH "GLASS MEMBRANE" IN THE ANTERIOR CHAMBER

REPORT OF A CASE

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Among the numerous hazards incurred by the fetus in its passage through the birth canal are those involving the ocular structures. Any factors which increase the stress on the fetal head during parturition will augment the chances of injury. These factors include narrowness or deformity of the maternal pelvis, prolonged labor and the use of obstetric forceps. In general, birth trauma involves the eyes of the newborn child by direct injury to the lids and eyeball, by the development of retinal and other intraocular hemorrhages and by intracranial damage to the visual and oculomotor pathways. The most frequent and serious injuries to the eye are the result of direct hurt by forceps. The left eye is implicated in the majority of instances, probably, as Lloyd [1] has pointed out, owing to the greater frequency of left occipitoanterior presentation and the greater chance of injury to the posteriorly placed left eye. The subject of ocular birth injuries has been thoroughly reviewed by Edgerton.[2]

Corneal injuries at birth are usually the result of compression of the globe between the roof and the superior margin of the orbit and the end of a poorly adjusted forceps blade. This pressure may affect the cornea in three ways: (1) by the formation of a diffuse corneal edema, which soon disappears; (2) by the development of a permanent diffuse opacity of the cornea as a result of edema and subsequent inflammatory reaction with proliferation of fibrous tissue, and (3) by the elaboration of permanent linear opacities of the posterior layers of the cornea. The last group is caused by rupture of Descemet's membrane and occasionally of the posterior layers of the corneal lamellae. In some of these cases,

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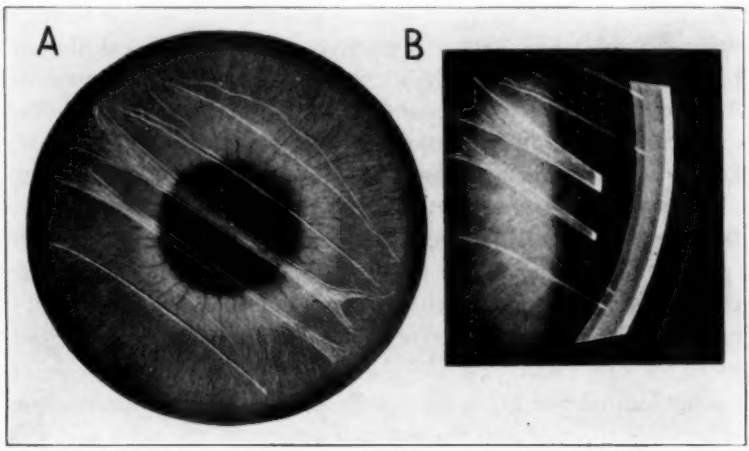
1. Lloyd, R. I.: Birth Injuries of the Cornea and Allied Conditions, Tr. Am. Ophth. Soc. **35**:212-220, 1937.

2. Edgerton, A. E.: Ocular Observations and Studies of the New-Born, with Review of Literature, Arch. Ophth. **11**:838-867 (May) 1934.

containing a so-called "glass membrane" in the anterior chamber, Descemet's membrane is stripped from the cornea, leaving a curled edge free in the anterior chamber, or is torn into strips extending across the anterior chamber and attached to the peripheral cornea at both extremities. Peters [3] first described serial microscopic sections of such an eye, with parallel ruptures of Descemet's membrane and four bands of this elastic structure with curled edges covered by endothelium lying in the anterior chamber. Such a "glass membrane" must be distinguished from that due to congenital anterior synechia and from the strands attached to the posterior surface of the cornea after inflammations. The literature dealing with corneal birth injuries has been fully investigated by Fewell [4] and by Lloyd.[1]



A, drawing of the cornea of the left eye to show multiple ruptures of Descemet's membrane. *B*, appearance of the left cornea and anterior chamber in the beam of the slit lamp.

REPORT OF CASE

Mrs. W. D., a 24 year old white stenographer, was referred to me by Dr. C. Dary Dunham for a routine ocular examination. The patient gave a history of defective vision of the left eye since birth. She had been told that her left eye had been injured by forceps during delivery and that a scar above her forehead resulted from a laceration at the same time.

Examination showed a normal emmetropic right eye. A small vertical scar was present at the hair line above the left side of the forehead. Vision of the left eye was equal to 20/400 and improved to 20/300, with correction of a

3. Peters, A.: Eine Verletzung der Hornhaut durch Zangenentbindung mit anatomischem Befund, Arch. f. Augenh. **56**:311-319, 1907.

4. Fewell, A. G.: Lesions of the Cornea Caused by Birth Trauma, Tr. Am. Ophth. Soc. **31**:329-344, 1933.

considerable amount of mixed astigmatism (+1.50 D. sphere combined with a −5.75 D. cylinder, axis 40), confirmed by study with the keratometer and by retinoscopy with homatropine cycloplegia. The visual fields were normal.

The left cornea showed slight haziness of its posterior layers and seven oblique linear opacities extending from the inferior temporal to the superior nasal quadrants (see figure on left of illustration). Study with the slit lamp and the corneal microscope revealed that the lower two and the upper three streaks had the characteristic appearance of ruptures of Descemet's membrane with the formation of glassy ridges on the posterior surface of the cornea. The two remaining linear bands consisted of ribbon-like structures stretched across the anterior chamber, attached to the cornea at their extremities (see figure on right of illustration). The bands had curled, rounded edges. It was apparent that the glassy strips extending across the anterior chamber were continuous with Descemet's membrane and consisted of ribbons torn away from the posterior cornea. The remaining structures in the interior of the left eye were normal.

SUMMARY

The subject of corneal birth injuries is briefly sketched, and an example is presented, the patient being a young white woman. She gave a history of injury by obstetric forceps at delivery. The involved left eye presented a high degree of corneal astigmatism, defective vision, multiple ruptures of Descemet's membrane and glassy strips of this structure extending across the anterior chamber. The abnormalities resulted from compression of the left eyeball during parturition.

DISCUSSION

DR. MILTON L. BERLINER: I think that such cases are very interesting, particularly on account of what actually happens pathologically. Several years ago I presented a paper on cysts of the cornea and showed how a retrocorneal cyst formed following a rupture of Descemet's membrane. What happened was that after the lower half of Descemet's membrane was stripped, the endothelium grew around the edges of the torn membrane to form a lining. A new Descemet's membrane was produced, which covered the gap. In the case I reported this was so extensive that an actual cyst formed on the postcorneal surface.

DR. CHARLES A. PERERA: I wish to thank Dr. Berliner for his discussion and to mention the fact that the edema of the cornea with permanent or temporary corneal opacity results from damage to the endothelium and posterior layers of the cornea.

CONJUNCTIVITIS IN ERYTHEMA EXUDATIVUM MULTIFORME

REPORT OF THREE CASES

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IOWA CITY

Erythema exudativum multiforme is not infrequently complicated by conjunctivitis, and this complication has led to blindness or even loss of the globes in many of the reported cases. In fact, the ocular involvement, although adventitious, is the most dangerous manifestation of the disease. Since the severity, type and extent of the generalized symptoms, cutaneous condition and reactions of the mucous membranes are variable, the scope of this disease is difficult to define.

The name erythema exudativum multiforme was proposed by Hebra [1] in 1866 to describe a cutaneous disease identified by erythema iris, herpes iris and variously shaped erythematous lesions of the skin. He observed that these eruptions occur at different stages in the malady and that all types may appear during the course of the disease. He stated that the most striking characteristic of this condition is its appearance on special parts of the body, i. e., the dorsal surfaces of the hands and feet, on which it was seen in every instance. Constitutional symptoms were noted only in exceptional cases, and no important complications or sequelae were described. Neither stomatitis nor ophthalmia was emphasized, but he noted that occasionally the mucous surfaces were affected.

Since this description, many additions have been made to the signs and symptoms of erythema exudativum multiforme. In 1937 Klauder [2] summarized these and divided the disease into two large classes, i. e., (1) erythema exudativum multiforme and (2) toxic erythema.

Erythema exudativum multiforme, a specific disease of unknown cause, is relapsing and involves the skin and mucous membranes. The distinctive lesions are annular erythemas with central clearing, erythema

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Part of a study being conducted under a grant from the John and Mary R. Markle Foundation.

1. Hebra, F.: On Diseases of the Skin, translated and edited by C. H. Fagge, London, New Sydenham Society, 1866, vol. 1.

2. Klauder, J. V.: Ectodermosis Erosiva Pluriorificialis, Arch. Dermat. & Syph. **36**:1067 (Nov.) 1937.

iris and herpes iris. The subtypes are the Hebra, the pluriorificial and the severe. The Hebra form is the most common, and the cutaneous lesions always involve the dorsal surfaces of the hands and feet. Constitutional symptoms and involvement of the mucous membrane may or may not be present. With the pluriorificial form there are constitutional symptoms, conjunctivitis, stomatitis, rhinitis and vesicular eruptions on the hands and feet. With the severe form (Stevens and Johnson [3]) there are constitutional symptoms, stomatitis, membranous conjunctivitis, hemorrhagic macular cutaneous lesions and leukopenia.

Toxic erythema resembles erythema exudativum multiforme but has known causes, such as systemic infection, drug intoxication or serum sickness. Visceral disease may be associated with it.

Ophthalmic complications in erythema exudativum multiforme were described first by Fuchs [4] (1876) in a patient with herpes iris and pseudomembranous conjunctivitis which produced no serious sequelae. Hanke [5] in 1901 reported a case in which there were pseudomembranes and corneal ulcerations. Barkan [6] observed a case in which purulent conjunctivitis occurred during one attack and pseudomembranous conjunctivitis with corneal ulcerations of both eyes in a second attack. In Stark's [7] case there were persistent pseudomembranes and corneal ulcers. Hartler [8] saw 2 patients with false membranes covering the tarsal conjunctiva. In 1 of these faint corneal turbidity developed; the other had no visual loss. Raffin [9] reported complicating pseudomembranous conjunctivitis with corneal involvement and scarring. In the 2 cases of purulent conjunctivitis reported by Stevens and Johnson the condition was complicated by corneal ulcers in three of the four eyes; in 1 case perforation occurred in both corneas. Rutherford [10] observed a case in which both globes showed pseudomembranous conjunctivitis, corneal ulceration and perforation. Corneal ulceration ending in blindness was

3. Stevens, A. M., and Johnson, F. C.: New Eruptive Fever Associated with Stomatitis and Ophthalmia, Am. J. Dis. Child. **24**:526 (Dec.) 1922.

4. Fuchs, E.: Herpes iris conjunctivae, Klin. Monatsbl. f. Augenh. **14**:333, 1876.

5. Hanke, V.: Der Herpes iris des Auges, Arch. f. Ophth. **52**:263, 1901.

6. Barkan, H.: Herpes Iris of Conjunctiva, Arch. Ophth. **42**:236, 1913.

7. Stark, H. H.: Chronic Membranous Conjunctivitis of Over Four Years' Duration, Am. J. Ophth. **1**:91, 1918.

8. Hartler, C. C.: Ueber die Kombination der Conjunctivitis et Stomatitis pseudomembranacea und ihr Verhältnis zum Erythema multiforme und Pemphigus, Klin. Monatsbl. f. Augenh. **67**:223, 1921.

9. Raffin, A.: Conjunctivitis, Rhinitis und Stomatitis aphthosa mit Erythema multiforme, Klin. Monatsbl. f. Augenh. **68**:216, 1922.

10. Rutherford, C. W.: Membranous Conjunctivitis with Loss of Eyeballs. J. A. M. A. **93**:1779 (Dec. 7) 1929.

the complication in the case Wheeler [11] reported. Bailey [12] described 3 cases: 1 of catarrhal conjunctivitis, corneal involvement and blindness, 1 of pseudomembranes and corneal involvement and 1 of purulent conjunctivitis, iritis, subconjunctival hemorrhages and permanent loss of vision. Ginandes [13] reported a case of pseudomembranous conjunctivitis followed by unilateral endophthalmitis and loss of the eye. Two cases of seropurulent conjunctivitis without sequelae were reported by Klauder, and in 2 cases observed by Edgar and Syverton [14] there was no permanent damage from the complicating conjunctivitis.

Duke-Elder [15] has classified ocular complications under the headings of catarrhal, purulent and pseudomembranous forms. The catarrhal form is characterized by mild conjunctivitis, which subsides simultaneously with the eruption and leaves no scars. In the purulent form, extreme conjunctival chemosis, corneal ulceration and perforation are not uncommon. The pseudomembranous form is the most devastating and most common ocular complication of erythema exudativum multiforme. The bulbar or palpebral conjunctiva or both may be covered by pseudomembranes. Symblepharon occurs when the process becomes severe. Corneal involvement is almost invariable and usually results in ulceration with perforation or permanent diffuse opacification. Recurrences are common.

REPORT OF CASES

CASE 1.—*History.*—An acutely ill white boy aged 9 years was admitted to the hospital on Oct. 21, 1938. His temperature was 104.4 F. One week before admission he complained of a cold, headache and burning eyes. Two days before admission a sore throat developed, the eyelids became swollen and a mucopurulent conjunctival discharge appeared. The day before admission "cold sores" appeared in the mouth and on the lips. At 10 a. m. the day of admission the patient became semistuporous; at noon he was given 10,000 units of diphtheria antitoxin because diphtheria was suspected, and at 7 p. m. he was admitted to the hospital.

This boy had a brother and 2 sisters, 4, 6 and 11 years old, respectively, who had had no similar trouble. No recent exposure to any contagious disease or condition similar to the present illness was reported.

Examination.—The patient was a well developed, poorly nourished white youth with several cutaneous lesions on the upper part of the chest and an equal number

11. Wheeler, J. M.: Destructive Purulent Ophthalmia Accompanying an Eruptive Fever with Stomatitis, Am. J. Ophth. **13**:508, 1930.

12. Bailey, J. H.: Lesions of the Cornea and Conjunctiva in Erythema Exudativum Multiforme (Hebra), Arch. Ophth. **6**:362 (Sept.) 1931.

13. Ginandes, G. J.: Eruptive Fever with Stomatitis and Ophthalmia, Am. J. Dis. Child. **49**:1148 (May) 1935.

14. Edgar, K. J., and Syverton, J. F.: Erythema Exudativum Multiforme with Ophthalmia and Stomatitis, J. Pediat. **12**:151, 1938.

15. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2.

on the back, thighs and face. There were several on the dorsal surface of the left foot and one on the plantar surface. Some were dusky, erythematous, maculopapular lesions, measuring 0.3 to 1 cm. in diameter, and others were characterized by a central thin-walled vesicle, 0.5 to 0.8 cm. in diameter, surrounded by a 2 mm. halo of hyperemia. The vesicle fluid was clear and straw colored.

A copious mucopurulent discharge exuded from between the red and swollen eyelids. The conjunctiva was chemotic over the globe, edematous in the fornices and beefy red on the lids. No conjunctival vesicles or follicles were seen. The cornea was clear and did not stain with fluorescein. No intraocular pathologic changes were observed.

Covering the lips and most of the mucous membrane of the oral cavity were thin-walled, large, flat vesicles, which in some areas had apparently ruptured

Fig. 1 (case 1).—Erythema exudativum multiforme showing conjunctivitis and involvement of the lips.

and had been replaced by yellowish gray pseudomembranes. These eruptions and psendomembranes were seen on the tonsillar pillars, the pharyngeal wall and extending over the epiglottis into the larynx. Bilaterally the cervical lymph glands were enlarged but not tender, and the preauricular glands were small and shotty.

The general physical examination revealed a few moist crackling rales over the lower portion of the chest and a barely palpable spleen.

Laboratory Examination.—The urine contained no blood, sugar or pus, but one specimen had a trace of albumin. Examination of the blood showed 4,400,000 red blood cells, 15 Gm. of hemoglobin and 21,600 white blood cells, of which 91 per cent were polymorphonuclear leukocytes and 9 per cent were lymphocytes. The Wassermann and Kline reactions were negative. There was no reaction to 0.00002 mg. of purified protein derivative of tuberculin given intradermally.

The conjunctiva was cultured on Löffler's medium, blood agar, ascitic fluid agar and chocolate agar, but no growth occurred under anaerobic or aerobic conditions. Conjunctival smears showed a few gram-positive rods with the morphologic character of Corynebacterium hofmanni.

One guinea pig was inoculated in the thigh with vesicle fluid and another with conjunctival discharge. No untoward reactions followed. Five months later the guinea pigs were inoculated intradermally with 0.001 Gm. of old tuberculin, but no reaction followed. Two rabbits were inoculated intracranially with similar material. Epithelium was scraped from another rabbit's cornea and the site inoculated with bleb fluid. The rabbit which received the vesicle fluid intracranially had a temperature of 103 F. on the third day after the inoculation, but the fever disappeared in a few hours. No abnormal reactions were noted in the other rabbits.

The pseudomembranes which later formed on the patient's tarsal conjunctivas were removed, fixed in Zenker's solution, sectioned and studied microscopically.

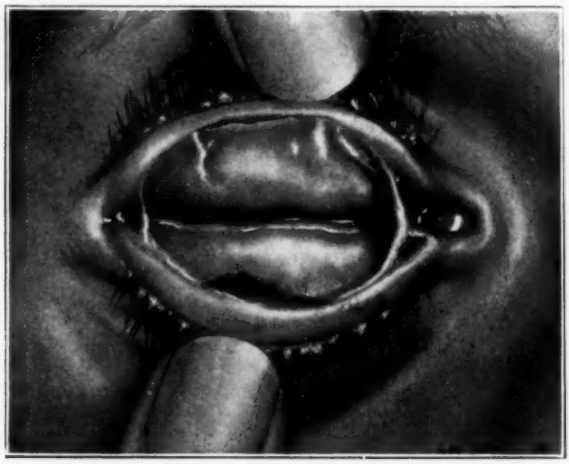

Fig. 2 (case 1).—Erythema exudativum multiforme showing pseudomembranous conjunctivitis.

The tissue consisted chiefly of round mononuclear cells enmeshed in a framework of closely packed fibrinous strands; however, a few fibroblasts and thin-walled blood vessels were present. The nuclei of the monocytes were variable in size and staining reaction, ranging from small deeply stained structures to large pale-staining or vacuolated bodies. Polymorphonuclear leukocytes were numerous throughout, and an occasional giant cell was seen. A few islands of necrotic epithelial cells were noted.

Course.—The temperature ran a septic course, reaching peaks of 104 F. the first three days. In the next two and one-half weeks it gradually subsided but often showed an afternoon rise to 101 F.

New cutaneous lesions continued to appear for a few days until they were sparsely scattered over most of the body. They appeared on the scalp, palms and plantar surfaces. The dorsal and ventral aspects of the body and extremities became equally peppered with lesions, many of which were vesicular. They were surrounded by a hyperemic halo, but after a few days the vesicle collapsed

and a red elevated ring remained. Itching or other symptoms were not associated with them. The lesions gradually healed, and at the time of the patient's discharge, thirty-three days after admission, only faintly pigmented spots remained.

The vesicles on the oral mucous membrane were replaced by gray ulcerous patches, which slowly disappeared. On the third hospital day pseudomembranes began to form on the palpebral conjunctiva and were stripped off with very little bleeding. However, the next day considerable bleeding followed their removal. They were gray, approximately 0.5 mm. thick and tenacious. Although in the beginning they covered only the palpebral conjunctiva, they soon extended over the fornices and onto the bulbar conjunctiva, but the cornea remained clear.

On the seventh hospital day the eyelids began to look less edematous and the conjunctival discharge was subsiding. By the ninth day the membranous material was practically gone, but adhesions began to form between the palpebral and the bulbar conjunctiva. These thin adhesions involved both fornices and canthi. To prevent symblepharon, the conjunctiva was anesthetized, and the young adhesions were broken down with a blunt glass rod. Considerable bleeding followed this manipulation. Boric acid ointment was put into the conjunctival sack after this procedure. It was necessary to tear down the adhesions daily for fifteen days. During the last week of hospitalization, the adhesions ceased to form, the conjunctiva healed and no shortening of the conjunctival sac was evident.

CASE 2.—*History.*—On Jan. 16, 1939 a white man aged 39, complaining of malaise, sore eyes, sore mouth and a cutaneous eruption, was admitted. He had been well until eleven days previously, when his eyes began to itch and burn. During the next few days vesicular lesions appeared on the lips, oral mucous membranes and urethral orifice, and lesions on the skin soon followed. Neoarsphenamine had been injected intravenously on January 10 for suspected Vincent's stomatitis, but new crops of lesions continued to appear. There was a slight burning sensation in the lesions. No history of similar attacks or of any contact with contagious or similar maladies was obtained.

Physical Examination.—This well nourished, well developed man had a temperature of 101 F. The fissured lips, which bled easily, were covered with crusts. On the tongue, buccal mucosa, hard and soft palates and anterior pillars were many erosions. These lesions were irregularly shaped and covered with a gray pseudomembrane. Similar erosions were found about the urethral meatus and extended over much of the glans penis. One lesion was seen on the rectal mucosa.

On the dorsal and ventral surfaces of the hands, forearms, feet, ankles, fingers and toes were many eruptions. A few were present on the buttocks and on the neck. These lesions, which varied from 0.5 to 1 cm. in diameter, were dusky erythematous papules, herpes iris and erythema iris.

The eyelids were slightly swollen. The palpebral conjunctiva was edematous and beefy red and was covered with mucopurulent material. One vesicle, 3 mm. in diameter, was seen on the lower palpebral conjunctiva of each eye. The bulbar conjunctivas were injected. Fluorescein did not stain the corneas, which were clear.

During hospitalization the patient received symptomatic treatment, and he was discharged after five days with practically normal skin and much improved mucous membranes.

Laboratory Examination.—Examination of the blood showed 6,650 leukocytes, with a normal differential count, 4,800,000 red blood cells, 15 Gm. of hemoglobin and a negative Wassermann reaction. The urine contained no blood, sugar or

Fig. 3 (case 2).—Erythema exudativum multiforme showing typical involvement of the palms.

Fig. 4 (case 2).—Erythema exudativum multiforme showing lesions on the dorsa of the hands.

albumin, but a few pus cells were seen with high power magnification. A Wright's stain of bleb fluid showed many polymorphonuclear leukocytes, some eosinophils and a few lymphocytes.

In cultures of conjunctival material a few colonies of Staphylococcus albus grew; no organisms were seen in smears of conjunctival material. The foot pads of a guinea pig were scarified and inoculated with bleb fluid, but no ill effects followed. Two guinea pigs were inoculated intraperitoneally with bleb fluid, but no untoward reaction occurred. Six weeks later 0.001 Gm. of old tuberculin was given intradermally to each guinea pig, with negative results.

CASE 3.—*History.*—On Feb. 18, 1939 an 8 year old white boy was admitted to the hospital because of malaise, a cutaneous disease, conjunctivitis, stomatitis and rhinitis. Six days previously a blister had appeared in the nose, and two days later the stomatitis, conjunctivitis and eruption had developed.

He had had two attacks similar to the present illness, but of less severity and without conjunctival involvement. The first occurred in May 1938, when lesions appeared on the hands, ears and oral mucous membrane and disappeared in approximately four weeks. After this illness the tonsils were removed because

Fig. 5 (case 2).—Erythema exudativum multiforme showing conjunctivitis and vesicle formation on the right lower lid.

the patient often complained of sore throat, fleeting joint pains and muscular cramps. The exanthema recurred in August 1938, with approximately the same involvement and period of convalescence.

Physical Examination.—The patient was a poorly nourished youth with a temperature of 100.2 F. General physical examination revealed a faint systolic nontransmitted murmur at the apex of the heart. The cutaneous lesions were ruptured and unruptured vesicular blebs, each surrounded by a narrow erythematous elevated border. They were present in great numbers on the palms and plantar surfaces but were thinly scattered on the skin of the face, legs and thighs. The lips were covered with bloody crusts, and on the mucous membrane of the mouth and nose were several ulcerated areas covered with gray pseudomembranes. A catarrhal exudate covered the mildly inflamed palpebral conjunctivas. There was a small crusted lesion on the margin of each lid of the right eye and two on the lower lid of the left. The corneas and bulbar conjunctivas appeared normal. No intraocular pathologic changes were seen.

A search for foci of infection revealed several carious deciduous teeth, which were extracted.

Convalescence progressed without further ocular or general involvement, and one month after admission the only remnants of the disease were a few incompletely healed oral lesions and faint pigmentation at the site of the eruptions.

Laboratory Examination.—The urine showed no blood, albumin or casts. Examination of the blood showed 2,900,000 erythrocytes, 4,600 leukocytes, with a normal differential count, 10 Gm. of hemoglobin and a negative Wassermann reaction. The conjunctivas were cultured on blood agar, but no growth occurred.

The guinea pigs which were inoculated with material from the patient in case 1 were given 2 cc. of whole blood intraperitoneally from the patient in case 3. The guinea pig which had been inoculated with conjunctival discharge from the patient in case 1 died four hours after receiving the blood. Autopsy revealed that the death was probably due to anaphylaxis. The other guinea pig had no ill effects. A rabbit was inoculated intracranially with 0.2 cc. of bleb fluid, but no reaction followed.

DIFFERENTIAL DIAGNOSIS

Among the conditions which must be differentiated from erythema exudativum multiforme are pemphigus, the human form of foot and mouth disease, erythema nodosum, dermatitis herpetiformis and epidermolysis bullosa.

Pemphigus shows large thin-walled bullae which develop in successive crops on apparently normal skin. It has a characteristic fetid odor. The constitutional disturbances vary greatly, but death often ensues. The coincidence of ocular and dermal pemphigus is rare and they may be separate entities, according to Sutton and Sutton.[16] The ocular involvement begins with catarrhal conjunctivitis followed by conjunctival vesicles or large macerated areas in the conjunctiva. Shrinkage of the conjunctiva follows, with symblepharon, ankyloblepharon and xerophthalmia.

The human form of foot and mouth disease is characterized by swelling and redness around the nails of the hands and feet, desquamation at the site of the vesicles on the fingers and toes and a dry burning sensation in the mouth. Conjunctivitis, rhinitis and balanitis, as well as stomatitis, may occur. The diagnosis is established by inoculation of scarified guinea pig foot pads with vesicle fluid.

Erythema nodosum may be associated with edema of the conjunctiva in the palpebral fissure, episcleritic bosses and nodules. The cutaneous lesions, which usually appear on the legs, are large flat reddish or purplish papules or nodules. Occasionally fever and arthritis are associated with the eruption. The cutaneous and conjunctival lesions disappear spontaneously.

The conjunctiva in dermatitis herpetiformis may show vesicles, erosions, pseudomembranes, keratinization, symblepharon, scarring and shrinking. Corneal leukomas may occur. The cutaneous lesions are

16. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939.

deeply seated vesicles on an erythematous base occurring in discrete collections widely scattered over the surface of the body. The eruption is chronic, remittent and intensely itchy.

The history of slight trauma of the skin followed by bullae in a patient who has a familial history of a similar disturbance would indicate epidermolysis bullosa. Epidermal cysts develop at the site of old lesions, and the finger and toe nails may atrophy. Ocular involvement is rare, but a vesicular eruption in subconjunctival tissue may occur, followed by pseudomembranes, conjunctival atrophy, symblepharon and corneal involvement.

COMMENT

The great multiplicity and diversity of the signs and symptoms of erythema exudativum multiforme make it easily understandable that many different names have been used to describe its manifestations.

Fuchs (1876) originated the term "herpes iris conjunctivae," which was later used by Hanke, Barkan and others. Rutherford classified his case as one of "membranous conjunctivitis with loss of the eyeballs." Wheeler chose the title "destructive purulent ophthalmia accompanying an eruptive fever with stomatitis." Stevens and Johnson reported 2 cases of "a new eruptive fever associated with stomatitis and ophthalmia." They were unable to classify the malady and felt that it represented a new entity. Ginandes used the same title and likewise stated the belief that the condition was a new disease and not an unusual form of erythema exudativum multiforme. Edgar and Syverton entitled their paper "Erythema Exudativum Multiforme with Ophthalmia and Stomatitis."

Rendu [17] (1916) and Fiessinger and Rendu [18] (1917) described a disease that was later named "ectodermosis erosiva pluriorificialis" and which has been considered a new entity by many French writers. Klauder classified it as a form of erythema exudativum multiforme.

In 1866 Hebra said, "In dermatology the vocabulary is even now too rich and there are in fact fewer diseases of the skin than names for those diseases." Perhaps the name erythema exudativum multiforme should still suffice, even though the scope of the disease has been much enlarged since Hebra's description. Regardless of the name used, the disease should be familiar to ophthalmologists, because the conjunctiva is often involved and the only serious sequela is ocular damage. Although most

17. Rendu, R.: Sur un syndrome caracterisé par l'inflammation simultanée de toutes les muqueuses externes coexistant avec une éruption varicelliforme puis purpurique des quatre membres, Rev. gén. de clin. et de thérap. **30**:351, 1916.

18. Fiessinger, N., and Rendu, R.: Sur un syndrome caracterisé par l'inflammation simultanée de toutes les muqueuses externes coexistant avec une éruption vésiculeuse des quatre membres, non douloureuse et non récidivante, Paris méd. **23**:54, 1917.

of the reports of the disease in the ophthalmic literature describe severe ocular damage, it should be emphasized that the conjunctivitis is usually mild but potentially destructive.

Bacterial and pathologic studies have added few clues to the etiologic nature of this disorder. Ramel [19] (1930), after inoculating guinea pigs with material from patients with erythema exudativum multiforme, found evidence that led him to state the belief that the tubercle bacillus was responsible. Barber [20] (1921) and others presented evidence that foci of streptococcic infection may be the cause, but the general present day opinion seems to agree with Hebra, who said, "I shall confess that the cause of these diseases (polymorphous erythemata) is altogether unknown to me."

SUMMARY

Three cases are reported of an exanthematous disease which has been classified under the name exudative form of erythema multiforme. Pertinent phases and descriptions from Hebra's original depiction, the present conception and the differential diagnosis of erythema exudativum multiforme are presented. The literature is reviewed briefly, with special attention to the outcome of the conjunctivitis and the various titles applied to this entity. The usual laboratory procedures and a limited number of animal inoculations failed to reveal an etiologic agent.

19. Ramel, E.: Some Observations on the Causation of Erythema Exudativum Multiforme (Hebra), Brit. J. Dermat. **42**:1, 1930.

20. Barber, H. W.: Protein Sensitization and Focal Sepsis in the Etiology of Certain Skin Affections, Guy's Hosp. Rep. **71**:385, 1921.

GELATINOUS CANCER OF THE CHOROID FOLLOWING CARCINOMA OF THE RECTUM

REPORT OF A CASE

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Statements regarding the frequency of metastatic cancer of the uvea show that the disease is not rare. Ask [1] in 1934 counted 211 published cases, in 157 of which the diagnosis was proved histologically. In 1936 Lemoine and McLeod [2] listed 230 cases, and in 1938 Bietti [3] found 28 additional cases. These statistics do not indicate the real frequency of metastatic carcinoma, since many ophthalmologic institutions do not publish reports of the more frequent types of metastasis in the uvea. The reports are reliable only in regard to the rare forms of metastatic cancer in the eye. Among these rare types, uveal tumors derived from the intestinal tract should be mentioned, especially those of the frequently occurring rectal carcinoma of which only a few cases of uveal metastasis have been reported. Arisawa [4] described in 1914 a case of medullary ulcerated carcinoma of the rectum with advanced colloid degeneration. The histologic features of the tumor in the choroid were scirrhous. Dixon and Benedict [5] in 1932 saw a woman with carcinoma of the rectum and a metastasis in the choroid of the same histologic type. In Kiep's [6] case of rectal carcinoma with choroid metastasis the tissue was not examined histologically.

The following case is the third in which the diagnosis has been verified histologically, and it seems to be the first observation of a typical metastatic gelatinous cancer in the choroid.[7]

From the Herman Knapp Memorial Eye Hospital.

1. Ask, O.: Zur Kenntnis der metastatischen Uvealkarzinome, Acta ophth. **12**: 308, 1934.

2. Lemoine, A. N., and McLeod, J.: Bilateral Metastatic Carcinoma of the Choroid, Arch. Ophth. **16**:804 (Nov.) 1936.

3. Bietti, G.: Metastasi coroideali precocissime di carcinomi primitivi latenti e problemi diagnostici che ne possono derivare, Boll. d'ocul. **17**:1638, 1938.

4. Arisawa, V.: Metastatisches Aderhautkarzinom bei latentem Primärtumor, Klin. Monatsbl. f. Augenh. **15**:695, 1914.

5. Dixon, C. F., and Benedict, W. L.: Adenocarcinoma of the Sigmoid with Metastasis to the Eye, Am. J. Surg. **15**:99, 1932.

6. Kiep, W. H.: Carcinoma of the Choroid Secondary to Carcinoma of the Rectum, Tr. Ophth. Soc. U. Kingdom **55**:566, 1935.

7. The case was clinically observed by Dr. A. Knapp, who provided the history.

REPORT OF CASE

History.—On Nov. 9, 1931, Mrs. S. B., aged 43 years, stated that she had noticed an impairment of vision in the left eye three months before. She had been operated on in 1922 by Dr. A. A. Berg for a tumor of the rectum,

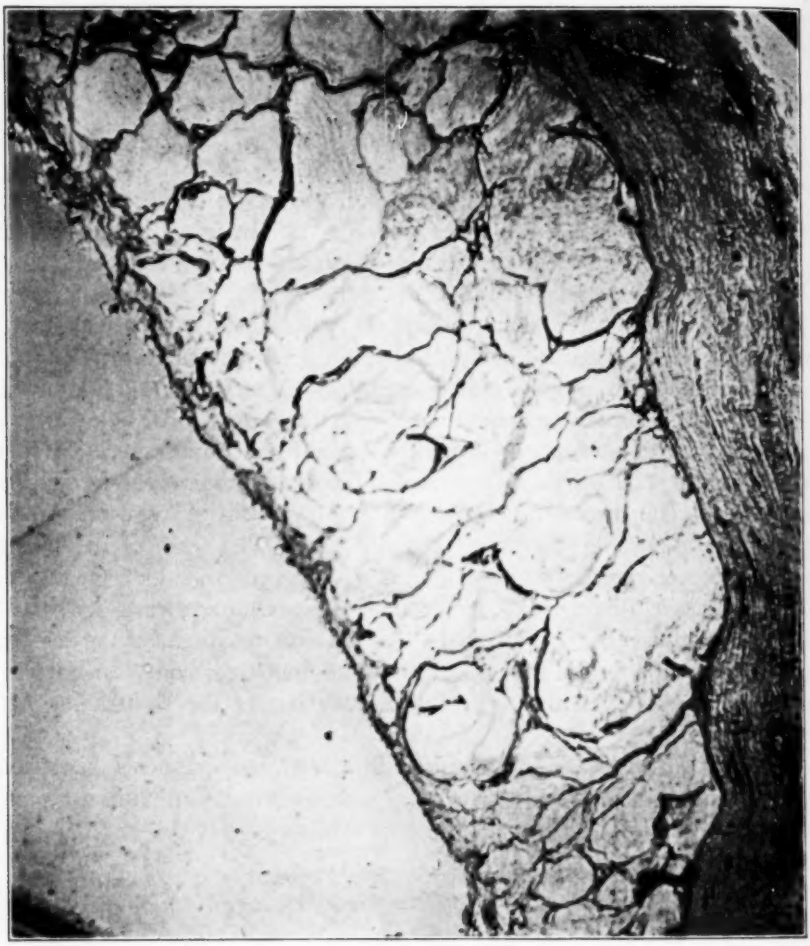

Fig. 1.—Photomicrograph of tumor tissue.

histologically an adenocarcinoma. On examination in April 1930 Dr. Berg found no sign of recurrence. Vision was 6/36; there was a large temporal field defect. In the nasal half of the fundus a grayish, broad, mottled, solid detachment extended to the disk and involved an area of about 5 disk diameters. The prominence was + 8 D. There was a serous detachment below. Enucleation was performed on November 12 because the primary character of the tumor could not be excluded. Two years later, in December 1933, the patient suffered from a metastasis in the liver and probably in the skull, and in January 1934 the condition was unimproved.

Three and a half years after the first symptoms of metastasis in the eye the patient was still alive, but she has not been examined again.

Histologic Examination.—The available sections were cut in a horizontal direction and passed through the optic nerve. The anterior part of the eye was normal. The retina was totally detached, but in the temporal half the detachment was the result of the fixative agent. In the nasal half a large serous detachment was evident. The inner layers of the retina were normal; the neuroepithelium was also to a great extent well preserved. In the area in front of the tumor, however, the cones and rods were degenerated. There was some pigment invasion into

Fig. 2.—Detail of figure 1.

this layer and the outer granular layer. In the nasal half the pigment epithelium was mostly destroyed. Remnant cells showed the usual forms of pigment epithelium degeneration. In the temporal half the pigment epithelium showed little change.

Tumor tissue took the place of the choroid in the nasal half, beginning at the nerve head and reaching the ora serrata. The tumor was of the usual flat dish-shaped type, with a maximal thickness of 2 mm. In the temporal half tumor tissue extended from the nerve head temporally 4 mm. and measured about 0.5 mm. in thickness.

The type of tumor tissue corresponded entirely to the histologic features of gelatinous cancer (fig. 1). Except in the peripheral area, it consisted of large

alveolar spaces of different forms and sizes. The fibrous walls between them were partly very fine trabeculae and partly thicker strands of connective tissue containing a moderate number of pigment cells. Staining with mucicarmine proved that the cavities were filled with mucous masses. A complete epithelial cover was absent in most alveoli. Remnants of the epithelium lining were seen in the form of strands of a cuboidal, darkly stained epithelium partly coating the walls and partly lying free in the mucus. Among the degenerate types of cells contained in the mucus were groups of indefinitely outlined cells with darkly stained protoplasm and almost invisible nuclei and others of the signet-ring type (fig. 2). Toward the periphery the tubular and alveolar cavities were well defined and lined with one to three layers of cylindric or flattened cells. The larger alveoli also contained mucous masses here. It may be concluded from the young, i. e., peripheral, parts that the tumor started in the middle layer of the choroid. In the temporal half the gelatinous degeneration was much less pronounced and the lamina vitrea was normal. In the nasal half it was not destroyed except for an area over the greatest elevation where the elastic membrane seemed to be interrupted. The growth, however, did not extend visibly into the retroretinal fluid.

Nasally from the disk gelatinous masses filled the lumen of the posterior ciliary vessels in the sclera, lining incompletely the inner surface of the walls with a single layer of epithelium. Other masses in the same stage of degeneration were found in and around the posterior ciliary vessels on the outer surface of the sclera.

COMMENT

In a great majority of cases metastatic tissue resembles the structure of the mother tumor. One may suppose, therefore, that the adenocarcinoma of the rectum was also gelatinous. The original sections of the rectal tumor are not available now. These growths have little tendency to metastasize. The very rare metastasis of rectal tumors to the eye has its parallel in the rare occurrence of metastasis in the brain. It is generally accepted that the action of the double filter in the blood transportation is responsible for this fact.

The ten year interval in this case between the discovery of the primary tumor and the development of the ocular metastasis is somewhat unusual, but cases of longer intervals have been reported previously. Another rare feature is the duration of life (three and one-half years) after the ocular metastasis, since clinical experience shows that survival generally does not exceed six months. Involvement of the posterior ciliary vessels shows the way of intrusion. The thrombosis of posterior ciliary vessels with tumor masses has also been described in several cases of choroidal metastasis of other origin.

CONGENITAL RETINAL FOLDS AND MICROCEPHALY

REPORT OF A CASE

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A congenital retinal fold is an anomaly characterized by a fold of retina which projects into the vitreous. It usually extends from the optic disk to the ora serrata. Microscopic studies show imperfect development of the layers of the retina within and without the fold. In the case to be reported there were congenital retinal folds similar to those described by others. In addition, the patient had microcephaly, microcrania and subnormal mentality. As far as I could determine, no other case has been reported with this combination of defects.

Thirty-eight cases of congenital retinal folds have been described in the literature. Cases belonging to this group were described under other titles by Sulzer [1] in 1888, Salffner [2] in 1902, Heine [3] in 1904, DeVries [4] in 1908, Holm [5] in 1923, Anacona [6] in 1935 and Hoffmann [7] in 1926. In 1928, Mann [8] described the condition as a congenital abnormality. In December 1935, Mann [9] reported on 8 eyes with this anomaly, which she defined as a new entity, calling it congenital retinal fold. Also in

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The case reported was studied by permission of Dr. Bernard Samuels at the New York Hospital.

1. Sulzer: Gefässhaltige überreste des hintern Abschnittes der gefässhaltigen fötalen Linsenkapsel beim Erwachsenen an einem Auge mit Membrana pupillaris perseverans und anderen Entwicklungsanomalien, Klin. Monatsbl. f. Augenh. **26:** 425, 1888.

2. Salffner, O.: Bulbus septatus, Arch. f. Ophth. **54:**552, 1902.

3. Heine, L.: Klinisches und Anatomisches über eine bisher unbekannte Missbildung des Auges. Angeborene Cystenretina, Arch. f. Ophth. **58:**38, 1904.

4. DeVries, W. M.: Arteria hyaloidea persistens, Nederl. tijdschr. v. geneesk. **44:**1399, 1908.

5. Holm, E.: Coloboma Corporis vitrei, Acta ophth. **1:**63, 1923.

6. Anacona, S.: A Case of Persistence of Primary Epithelial Optic Papilla (von Szily), Nederl. tijdschr. v. geneesk. **79:**135, 1935.

7. Hoffmann, H.: Ueber eine seltene Strangbildung im Augenhintergrund, Klin. Monatsbl. f. Augenh. **77:**370, 1926.

8. Mann, I. C.: A Case of Congenital Abnormality of the Retina, Tr. Ophth. Soc. U. Kingdom **48:**383, 1928.

9. Mann, I. C.: Congenital Retinal Fold, Brit. J. Ophth. **19:**641, 1935.

December 1935, Weve [10] reported 8 similar cases and called the anomaly ablatio falciformis congenita. I prefer Mann's title, as she had precedence and it is simple and descriptive. Since 1935, Mann [11] and Weve [12] have added other cases, and in addition, reports have come from Kiewe,[13] Iles,[14] Evans,[15] Malbran and Adrogue [16] and Theodore and Ziporkes.[17] Tillema [18] reported a unilateral anomaly that had some resemblance to a congenital retinal fold but was apparently secondary to an abscess in the vitreous.

Bilateral and unilateral retinal folds have been reported. With the bilateral anomaly there is usually a symmetric arrangement of the folds. While the condition occurs most often in isolated cases, a familial incidence has been observed. Consanguinity has been noted in some instances.

REPORT OF CASE

N. D., a youth aged 19, had always had poor vision. His mother and father were first cousins. His appearance was peculiar at birth, and his parents were soon aware of his defective vision. At first he was thought to be blind. At the age of 4 months he was examined by Dr. Alfred Wiener, who has placed at my disposal the data set down by him. At that time the patient's skull was microcephalic. Its circumference was 14¾ inches (37.4 cm.); the normal is 17 inches (43 cm.). There was nystagmus. The fundi could not be seen clearly, but each eye showed a white reflex in one area and a red reflex in another. Vision was apparently very poor. Roentgenograms of the skull at 4 months showed that the fontanels were closed. (Normally the posterior fontanel closes at 6 months and the anterior fontanel at 18 months.) A later examination by Dr. Wiener showed no change except that there was mental retardation.

The patient began to walk and talk at the age of 2 years. He did not feed himself until he was 6 years old. He began to dress himself at that age. He attended a sight conservation class in elementary school, attaining the sixth grade when he was 16 (normally attained at 11 years).

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10. Weve, H.: Ueber Ablatio falciformis congenita, Arch. f. Augenh. **109**:371, 1935.

11. Mann, I. C.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, p. 157.

12. Weve, H.: Ablatio Falciformis Congenita (Retinal Fold), Brit. J. Ophth. **22**:456, 1938.

13. Kiewe, P.: Beitrag zur Kenntnis der angeborenen Missbildungen des menschlichen Auges, Arch. f. Ophth. **135**:220, 1936.

14. Iles, A. E.: Congenital Retinal Fold, Proc. Roy. Soc. Med. **29**:390, 1936.

15. Evans, P. J.: Congenital Fold of the Retina, Tr. Ophth. Soc. U. Kingdom **56**:344, 1936.

16. Malbran, J., and Adrogue, E.: Pliegues congénitos de la retina, Arch. de oftal. de Buenos Aires **12**:500, 1937.

17. Theodore, F. H., and Ziporkes, J.: Congenital Retinal Fold, Arch. Ophth. **23**:1188 (June) 1940.

18. Tillema, A.: Infantile and Congenital Retinal Fold, Brit. J. Ophth. **21**:94, 1937.

Physical Examination.—The patient was of medium height and slim, with narrow shoulders, which he carried with a slight stoop. The neck was long and thin.

The face was small. The head was still smaller in proportion to the face. The head looked abnormal, with a long sloping forehead that arched backward at a considerable angle. The ears were placed high on the head. The chin was receding (fig. 1).

The greatest circumference of the skull was 19¼ inches (48.2 cm.). The vertical distance from the middle of the ear canal to the top of the head was 4 inches (10 cm.).

Eyes: The eyes were deep set and close together. There was a left convergent squint. The interpupillary distance was 53 mm. There was a horizontal rotary nystagmus, which was worse when the right eye was covered. Vision in the right eye was 7/200 and in the left eye 4/200, unimproved by glasses.

Fig. 1.—Patient with congenital retinal folds and microcephaly.

The cornea was small, with a horizontal diameter of 10 mm. The right pupil was slightly larger than the left. Both reacted promptly to light and in accommodation.

The right lens was clear.

The left lens had a number of sharply localized opacities (fig. 2). On the nasal side there was a dense triangular opacity which study with the slit lamp showed to be in the deeper layer of the adult nucleus. In the temporal and lower sectors there was an irregular semitransparent opacity in the posterior capsular and subcapsular zone. Behind it, a delicate irregular mass extended backward into the vitreous. From this mass a number of fine wavy lines interlaced extensively on the nasal side of the posterior surface of the lens. The thickness of the lines was uniform. They appeared to be shrunken blood vessels, representing fetal remains of the tunica vasculosa lentis. The opacity in the temporal and lower sectors of the lens and the mass behind it were in the same meridian as the retinal fold.

Fig. 2.—Enlarged view of the left lens.

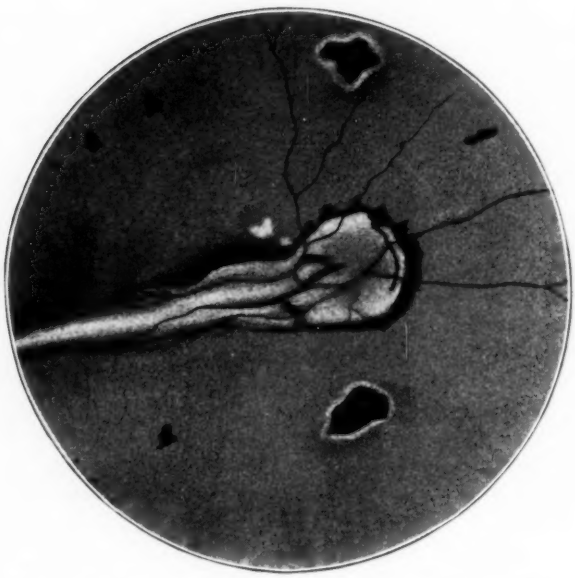

Fig. 3.—Fundus of the right eye with congenital retinal fold.

The retinal fold in each eye appeared as a broad gray band which extended from the disk to the periphery on the temporal side, slightly below the horizontal meridian. It was similar and symmetric in arrangement and position in the two eyes (fig. 3).

The retinal fold continued to the surface of the disk without any intervening margin. The fold gradually and indistinctly merged with the disk. The retinal fold in general was gray; however, in the region of the disk, where it became gradually flattened to the level of the surrounding retina, it took on a pink hue. The area of the disk was further distinguished by the origin there of the retinal vessels. As the fold extended away from the disk it assumed a tubular shape.

The retinal vessels were anomalous in size and distribution. Most of the branches lay on the fold. They ran over about half the visible length of the fold and then disappeared over the sides. Very few vessels supplied the rest of the retina. The number of visible vessels was much less than normal. The paucity

Fig. 4.—Roentgenogram of the patient's skull.

of vessels was further accentuated by their marked attenuation; they appeared to be mere threads. The branches seen were of such similar size and color that it was almost impossible to distinguish arteries from veins.

The gray of the retinal fold stood out in contrast against the pink of the rest of the fundus. The retina outside the fold was also striking because of its glazed and atrophic appearance and because of pigment deposits. There were a number of densely pigmented spots, irregularly placed. Around a few of the larger deposits was a white halo. There was a zone of dark pigmentation that formed a border around the disk and around the edge of the fold near the disk.

No sign of a macula could be found in either eye. The fold occupied the region normally taken by the macula. That, of course, was an added reason for the poor vision.

The field of vision was difficult to determine, owing to nystagmus and poor fixation. There was concentric contraction of the fields. Colors in large test objects were recognized.

In other respects physical examination gave negative results. Neurologic examination likewise gave negative results. All the normal reflexes were present, and no abnormal ones were noted.

The general attitude of the patient was pleasant and cooperative. He was interested in his surroundings and amused by his examination. His manner was kindly and gentle. Intelligence tests indicated a mental age of about 8 years. His chronologic age was 19.

Roentgen Examination.—A roentgenogram of his skull showed microcephaly (fig. 4). The cranial vault was disproportionately small compared to the facial bones. The cranial vault was thick, especially in the region of the parietal and occipital squamous bone. There was, however, some accentuation of the digitate impressions, and the vascular grooves were rather wide. The pneumatic cavities were excessively large. The anterior fossa of the base of the skull was flat. The sella was rather shallow and small. There was no evidence of pathologic change within the orbits, and there was no change in the appearance of the optic foramens.

His parents were first cousins. I examined them but found no defect. His brother was normal except that the shape of his head resembled that of the patient's. In an examination of 40 of his relatives no other case of retinal fold was found.

ANATOMIC STUDIES

Most of the cases reported in the literature were discovered in early infancy. The retinal fold, especially when unilateral and irregular, aroused the suspicion of glioma. On this account many of the globes were enucleated. The correct diagnosis was established by microscopic study. Since the entity was first defined, in 1935, many instances have been reported. It is likely that congenital retinal fold was given other diagnoses before. It would be of interest to go through the collections of ocular slides previously labeled pseudoglioma or congenital retinal detachment to see whether any of the conditions were actually congenital retinal folds.

Microscopic studies have shown that this anomaly is characterized by elevations and folds of the retina which project into the vitreous. The elevations are of varied height, usually only a few millimeters. The underlying pigment epithelium and the choroid are not affected. The surface of the fold is usually rounded; occasionally it has sharp edges. The fold usually begins at the disk and extends outward, in most cases reaching the ora serrata. However, the fold may be only a few millimeters long and may be away from the disk. The favorite meridian is the lower temporal, as in the case presented, though the folds have been observed in all meridians. No explanation has been given for the localization of most folds in the lower temporal meridian. In some cases the folds are unilateral, but in most they are bilateral. The bilateral folds are usually symmetric.

In all cases studied, remains of hyaloid blood vessels have been found adherent to the retinal fold. These strands have been traced forward to the lens, apparently connected to the vasa hyaloidea and the remains

of the tunica vasculosa lentis. Mann's theory is that this abnormal attachment and persistence of the hyaloid vessels pulls the retina away from its normal position and produces the fold. She predicates an abnormal attachment of the primary vitreous to the retina.

The retina in the fold is abnormal, its layers disturbed and distorted, with rosette formation. The remainder of the retina is also abnormal and imperfectly differentiated. The ganglion cell layer is incomplete; the rods and cones are poorly developed.

The color of the fold is pale gray, similar to the color of a detached retina. The retinal blood vessels are seen in sharp contrast against the gray fold. The attenuation of the blood vessels is probably associated with the lack of development of the retina.

In most of the cases processes extend from the fold to the posterior surface of the lens. They are associated with localized lens opacities. In my case the chief opacity was found in the same meridian as the retinal fold.

Vision is usually poor, even in those cases in which the macular area is not affected. It is worse when the fold involves the macula, as in this case. The poor vision probably accounts for the nystagmus. Squint is common. Other ocular anomalies have been observed in association with retinal fold, such as coloboma of the iris and persistent pupillary membranes.

HEREDITY

Weve found a number of cases in members of the same family. He studied twins in whom all four eyes were similarly affected. Consanguinity has been noted in several instances. In some cases of pronounced retinal fold, Weve [12] found other members of the family with only slight or suggestive folds. My patient was the son of first cousins. I examined 40 of his relatives but found no other retinal fold. The defect appears to be a recessive characteristic.

ASSOCIATION OF RETINA AND BRAIN

In addition to the retinal folds, the patient presented had microcrania, microcephaly and subnormal mentality. Roentgenograms at the age of 4 months showed microcephaly and premature closure of the fontanels. Early closure of the anterior fontanel is usually associated with microcephaly and arrested cerebral development. It is generally accepted that as the brain ceases to grow so does the skull. If the skull became fixed while the brain continued to grow, there would be increased intracranial pressure and damage to the brain. One would expect to see signs of previous papilledema or, possibly, optic atrophy. There might be signs of focal injury, such as paralysis, anesthesias or disturbed or abnormal reflexes. The roentgenogram of the skull would show marked

increase in its digitations. These signs were not found in the present case. Therefore, it seems that in the case presented the brain did not develop, and, as a consequence, the head also stayed small.

The association of abnormality of the brain and abnormality of the retina is not surprising in view of the close embryologic relation of these structures. The association of degeneration of the two structures in cerebromacular degenerations and in some cases of retinitis pigmentosa is well known. In this connection, it is of interest to note that Weve [12] reported on a family group of whom some had congenital retinal folds and some others had atypical retinitis pigmentosa.

In 1923, Holm [5] reported as coloboma of the vitreous a condition which is now recognized as typical congenital retinal fold in both eyes. He mentioned that the patient had the expression of an imbecile. None of the other reports of congenital retinal fold made any mention of the appearance of the face or head or of the mentality of the patient. It would be of interest if all the cases were reviewed in order to obtain this information.

SUMMARY

Congenital retinal fold is an anomaly of the eye characterized by a fold of retina which projects into the vitreous. One end of the fold is usually at the disk and the other at the ora serrata.

A typical case of bilateral, symmetric retinal folds is presented. In addition to this rare anomaly the patient had microcrania, microcephaly and subnormal mentality.

A RICKETTSIA-LIKE ORGANISM OF THE CONJUNCTIVAL EPITHELIUM OF PIGS

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In 1907 Halberstädter and von Prowazek first described the cellular inclusions associated with trachoma. In 1909 Stargardt [1] found similar inclusions in cases of blenorrhoea neonatorum; indeed, the bodies of inclusion blenorrhea cannot be distinguished from those of trachoma on morphologic grounds. Leber and von Prowazek [2] in 1912 published a report on a disease of man, probably trachoma, in the South Sea islands and called the inclusions Lyozoon atrophicans, a species of Chlamydozoa.

Shortly after these discoveries were made Uhlenhuth and Böing,[3] in 1910, stated that they had found bodies in the conjunctival epithelium of pigs and that these bodies closely resembled the inclusions of trachoma and blenorrhoea neonatorum. From this time onward various German workers [4] linked these structures, closely or loosely, with the virus of swine fever or hog cholera. These hazy perceptions still persist in many quarters. Von Buzna,[5] however, failed to detect the inclusions in cases of hog cholera examined by himself.

This study was made while the author was working as a Commonwealth Fund Service Fellow in Dr. E. V. Cowdry's laboratory in the medical school of Washington University, St. Louis.

1. Stargardt, cited by Findlay, G. M., in Doerr, R., and Hallauer, C.: Virusforschung, Berlin, A. Hirschwald, 1938, pt. 1, p. 309.

2. Leber, A., and von Prowazek, S.: Epitheliosis desquamativa conjunctivae der Südsee (Lyozoon atrophicans), in von Prowazek, S.: Handbuch der Pathogenen Protozoen, Leipzig, Johann Ambrosius Barth, 1912, vol. 1, pp. 162-171.

3. Uhlenhuth, P., and Böing, W.: Chlamydozoenbefunde bei Schweinepest, Berl. klin. Wchnschr. **47**:1514, 1910.

4. Böing, W.: Ueber Zelleinschlüsse bei Trachom und Conjunctivitiden, Arb. a. d. k. Gesndhtsamte. **40**:235-244, 1912. Uhlenhuth, P.: Experimentelle Untersuchungen über die Schweinepest, Centralbl. f. Bakt. (Abt. 1) **64**:151-165, 1912. Uhlenhuth, P., and Haendel, L., in Kolle, W., and von Wassermann, A.: Handbuch der pathogenen Mikroorganismen, Jena, Gustav Fischer, 1913, vol. 6, pp. 361-364. Uhlenhuth, P.; Miessner, H., and Geiger, W., in Kolle, W.; Kraus, R., and Uhlenhuth, P.: Handbuch der pathogenen Mikroorganismen, ed. 3, Jena, Gustav Fischer, 1929, vol. 9, pp. 308-309.

5. von Buzna, cited by Geiger, W., and Gildemeister, E.; Haagen, E., and Waldmann, O.: Handbuch der Viruskrankheiten, Jena, Gustav Fischer, 1939, vol. 1, p. 553.

Meyer [6] was the first to see the bodies in the United States and then only in 2 pigs. Both animals had hog cholera. Then Himmelberger [7] in Kentucky in 1916 reported the finding of inclusions in 95 per cent of pigs examined during the first stages of swine fever, but he found no evidence of their parasitic relation to the disease. Himmelberger's description of the inclusions is so meager and the only illustra-

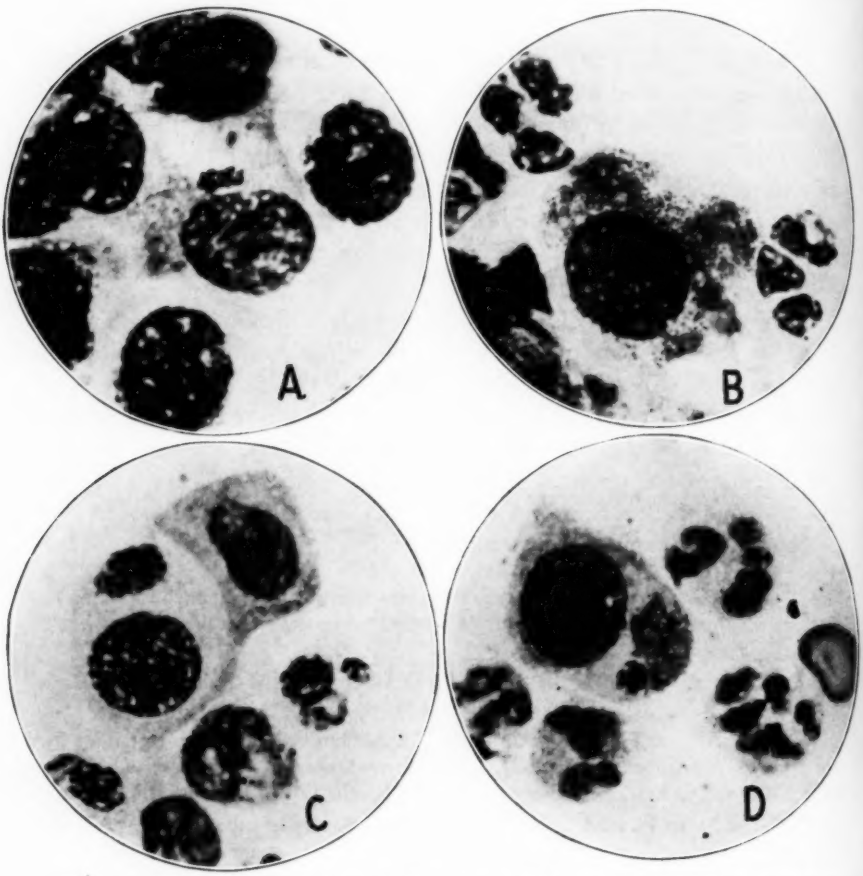

Fig. 1.—Inclusion blenorrhea (child) (× 1,400). *A*, conjunctival epithelial cell with a small colony of initial bodies above the nucleus. *B*, conjunctival epithelial cell packed loosely with elementary bodies. *C*, conjunctival epithelial cell with a colony of mixed initial and elementary bodies above the nucleus. *D*, conjunctival epithelial cell containing a small colony of initial bodies next to a large colony of elementary bodies.

6. Meyer, K. F.: Proc. Tenth Internat. Vet. Cong. **3**:271, 1914.

7. Himmelberger, L. R.: Cell Inclusions in Hog Cholera, J. Am. Vet. M. A. **1**:450-453, 1916.

tion in his article is so poor that some doubt must unfortunately remain as to whether he actually saw the bodies described in Germany.

By 1934 I [8] had found Rickettsia-like organisms associated with conjunctivitis of the sheep, goat and ox. These experiences, together

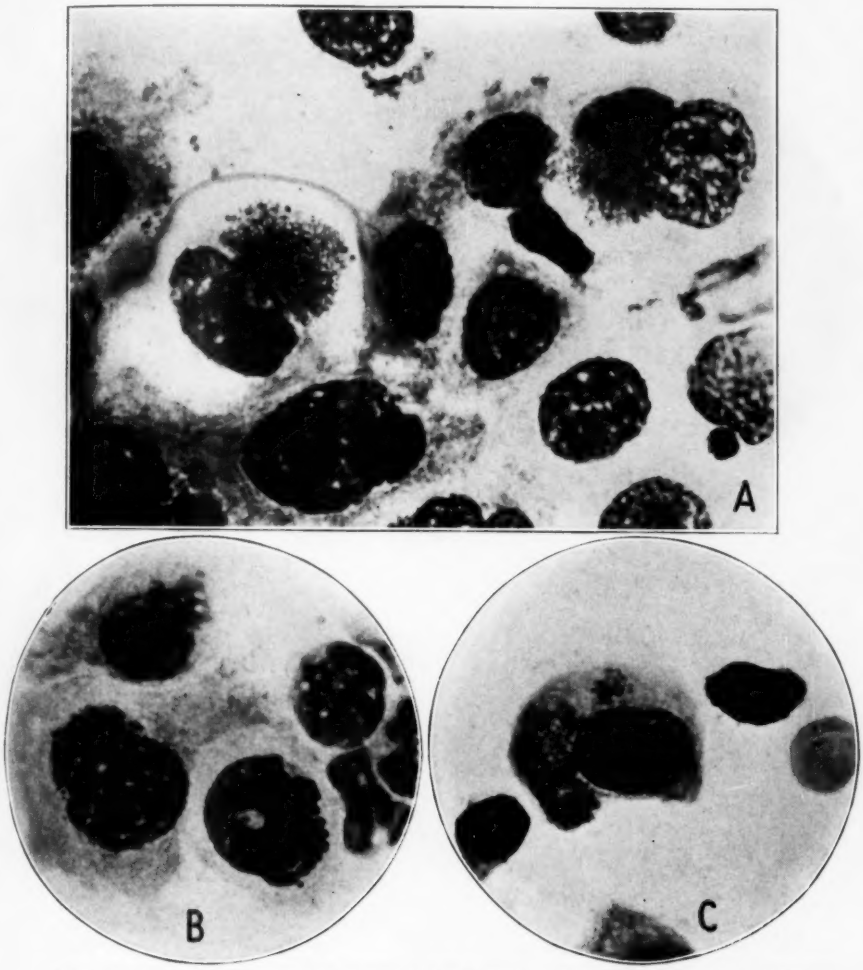

Fig. 2.—Inclusion blenorrhea (child) (× 1,400). *A*, two conjunctival epithelial cells, each containing a large colony of elementary bodies capping the nucleus. *B*, conjunctival epithelial cells. To the left of the nucleus on the left is a large mass of elementary bodies. To the right of the nucleus on the lower right is a mass of large initial bodies. *C*, conjunctival epithelial cell. Above the nucleus is a small colony of initial bodies, and to the left of the nucleus is a large clump of elementary bodies.

8. Coles, J. D. W. A.: (*a*) A Rickettsia-Like Organism in the Conjunctiva of Sheep, Seventeenth Report of the Director of Veterinary Services and Animal

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with the fact that Uhlenhuth in 1912 had admitted finding the inclusions in a small percentage of pigs without swine fever, convinced me that the German and other workers had been dealing not only with hog cholera but also with a superimposed infection. This concomitant disease should, I thought, be classed with infectious ophthalmia of cattle,

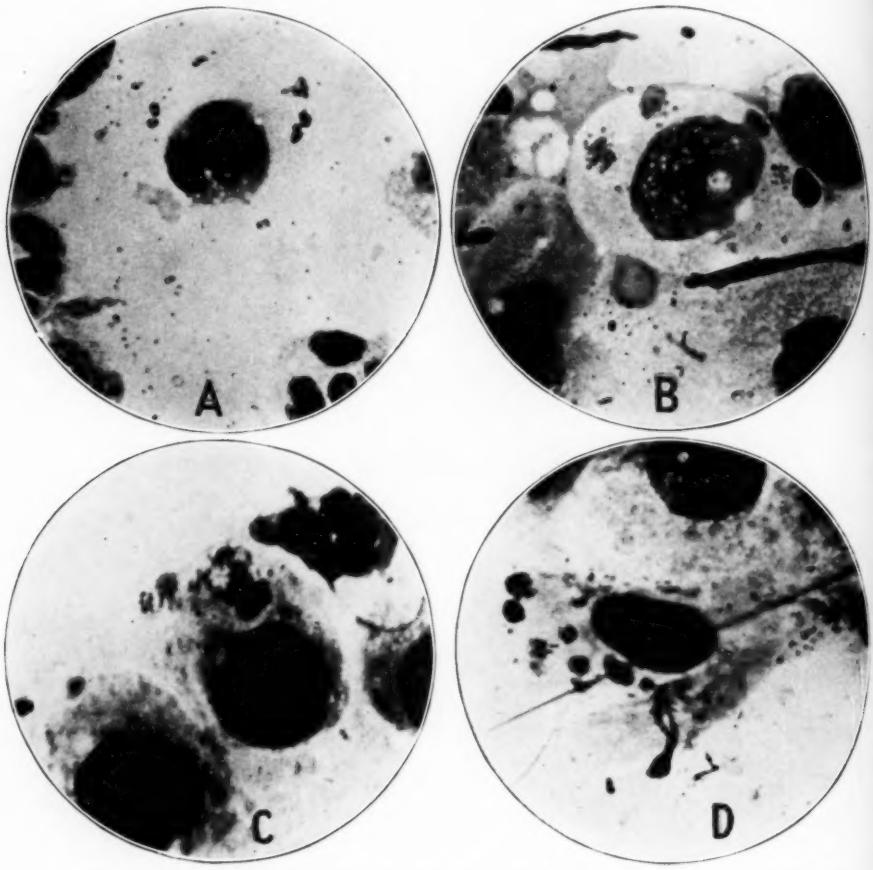

Fig. 3.—*A*, inclusion blenorrhea (child) (× 1,400). Bipolar initial bodies. *B*, *C* and *D*, conjunctival epithelium (pig) (× 1,400). *B*, five colonies of elementary bodies; the granules are easily seen in three. *C*, cell showing at least seven colonies, some of which appear to be running into each other. *D*, cell showing at least nine colonies. There are also scattered granules along the upper and right margins.

Industry, Union of South Africa, 1931, pp. 175-186; (*b*) A Rickettsia-Like Organism and an Unknown Intracellular Organism of the Conjunctival Epithelium of Goats, Onderstepoort, J. Vet. Sc. & Animal Industry **4**:389-395, 1935; (*c*) A Rickettsia-Like Organism of the Conjunctival Epithelium of Cattle, J. South African Vet. M. A. **7**:221-225, 1936.

sheep and goats. Also, as is now known, there is close similarity to a new form of conjunctivitis of the domestic fowl.[9]

During my visit to the United States, Dr. Thygeson told me of his repeated failures to find the conjunctival inclusions of hog cholera. In

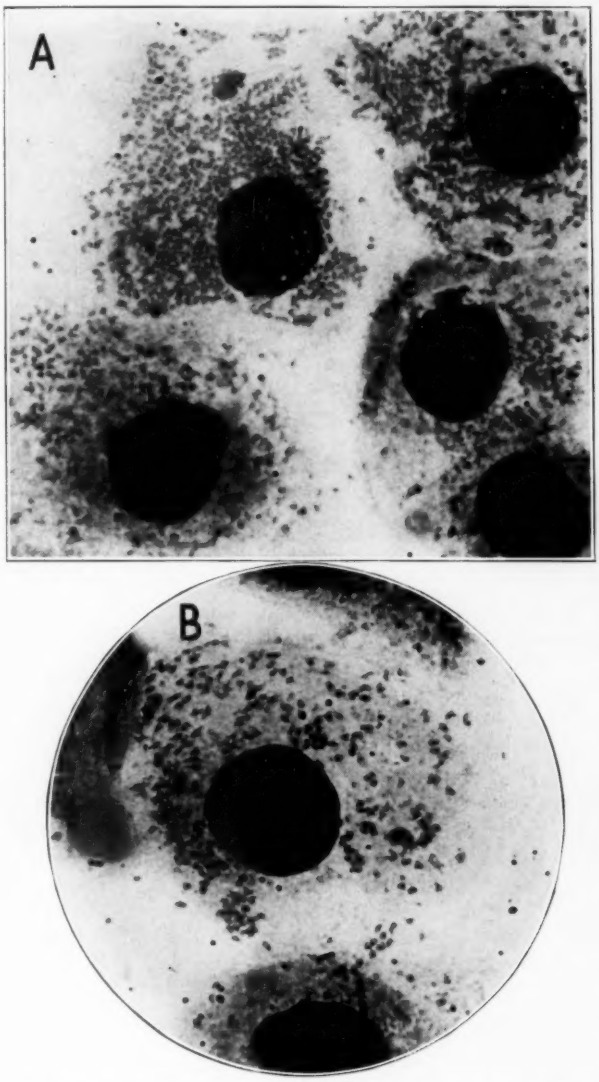

Fig. 4.—Conjunctival epithelium (pig) (× 1,400). A, cells packed with Rickettsia-like organisms. *B*, cell containing many granules, most of which are shaped like boomerangs.

9. Coles, J. D. W. A.: To be published.

December 1934 I attended a large gathering of veterinarians in Galesburg, Ill., and asked if any of them had ever seen pigs suffering from conjunctivitis alone. Only 2 could help me, and this indicates that

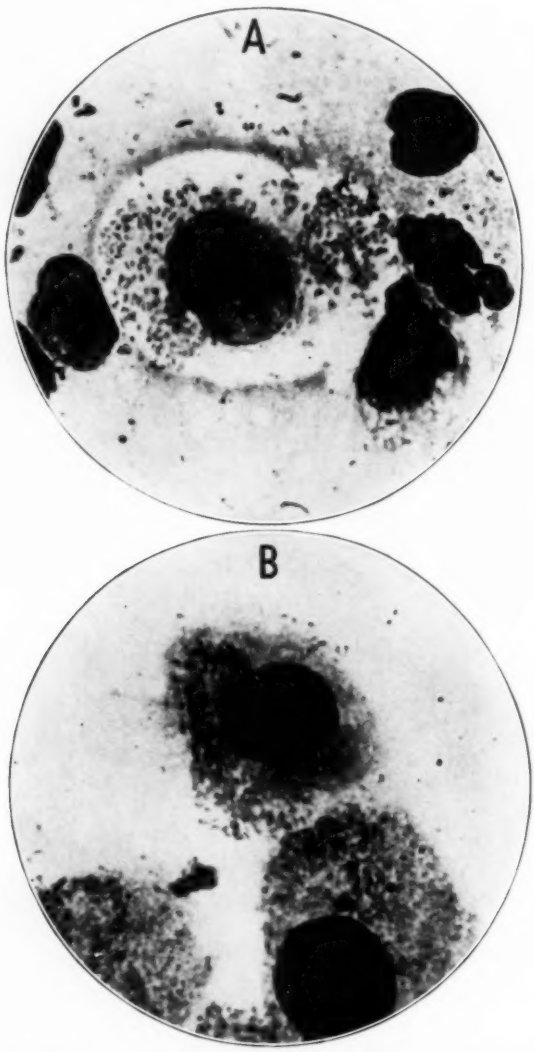

Fig. 5.—Conjunctival epithelium (pig) (× 1,400). *A*, cell containing many Rickettsia-like organisms. *B*, cells containing masses of Rickettsia-like organisms. In the top cell the granules are in a compact colony fitting snugly to the nucleus around half its circumference.

the conjunctivitis is usually so mild and so easily overlooked that the farmers never worry enough to consult their veterinarians about it.

In due course Dr. J. D. Ray of Omaha and Dr. C. L. Campbell of St. Louis found the cases I desired and generously collected material for me. This material forms the basis of the present discourse. It is important to add that Dr. Ray subsequently proved some of the infected pigs to be susceptible to hog cholera.

The descriptions given by the German workers may convey to some extent a false impression, owing to the fact that nearly all their studies were made on pigs with swine fever.

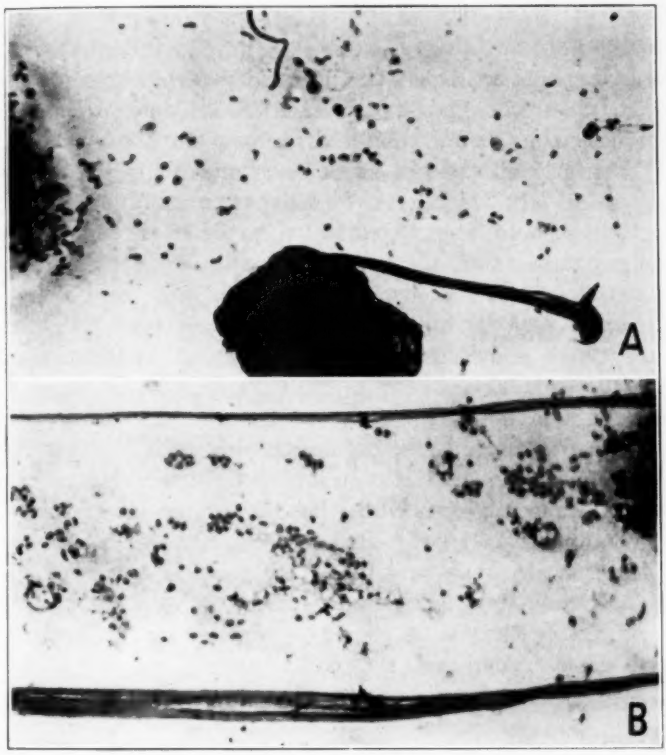

Fig. 6.—*A*, conjunctival epithelium (pig) (× 1,400). Infected cell on left. The free-lying organisms varied in shape and color (Giemsa stain). Many of the larger granules stained light blue and corresponded to initial bodies. The smaller granules stained like chromatin and were equivalent to elementary bodies. *B*, conjunctival smear (pig) (× 1,400). Free-lying initial and elementary bodies with many in-between forms. Bipolar organisms can be seen.

Uhlenhuth in 1910 made conjunctival preparations at a time when the animals had hog cholera. There was a purulent discharge from the eyes; the lids were edematous and stuck together, and inclusions were present. At the same time Böing succeeded in transmitting the infection

from eye to eye; the incubation period was seventy-two hours. He noted that the granules in the inclusions were coarser than those in the case of trachoma and that the pig inclusions were sometimes situated at considerable distances from the nuclei of the host cells.

In 1912 Uhlenhuth found inclusions in all pigs with conjunctivitis, and he also observed that the individual granules were generally bigger than in animals with trachoma. Though he recorded the presence of the bodies in about 3 per cent of animals not suffering from hog cholera, he observed them in nearly all pigs with the disease, particularly from the fifth to the tenth day of illness and sometimes even during the incubation period.

Uhlenhuth and Haendel in 1913 added a few details to what had already been written. They again remarked on the purulent conjunctivitis characterizing the infection and restated that the inclusions could be found in nearly all cases of swine fever and might even have some diagnostic value. In animals infected experimentally with the cholera virus, inclusions could be expected in five to six days; the same applied to piglets put into a cholera-infected sty. In many eyes the inclusions were extraordinarily numerous; in others they were rare. The bodies could seldom be seen for more than four to five consecutive days, even though they were numerous in the beginning. They were often gone in two or three days. Sometimes they reappeared in small numbers for a day or two later on. The inclusions could be demonstrated twenty-four hours after death, but by the forty-eighth hour they had disappeared on account of the postmortem changes. Not infrequently inclusions were present even when the conjunctiva showed no obvious signs of inflammation. I have often witnessed this phenomenon in the case of sheep, cattle, goats and fowls, but there is always microscopic evidence of inflammation if the organisms are at all numerous, as they usually are during the active stages of the diseases in these species, with the possible exception of the ox.

Uhlenhuth and his co-workers did not succeed in transmitting the infection to monkeys, rabbits, guinea pigs, rats, goats, dogs, horses, donkeys and cattle. Unlike Böing, they failed to effect pig to pig transmission. This does not surprise me. All my early attempts to infect fowls from fowls ended in failure, and it was only when I scraped off the diseased conjunctival epithelium with a bone curet, or even a pledget of cotton wool held by forceps, and then rubbed it stiffly on the surface of the healthy epithelium that the typical conjunctivitis developed in the fowls. Instilling the infection into a normal fowl's eye was useless. Uhlenhuth and Haendel concluded by stating that the true significance of the inclusions remained in doubt.

The observations made by Ray, Campbell and myself in the United States tend to show that the disease in pigs is limited to an acute or sub-

acute conjunctivitis involving one or both eyes. In fairly severe forms there is a slight purulent discharge. The cornea seems to be seldom, if ever, inflamed. The eyelids may be edematous.

The veterinary literature is singularly silent on the disease, and for this reason it is probably safe to assume that decided lacrimation, photophobia and gumming of the lids are unusual symptoms. Little is known about the duration of the condition. It seems tolerably certain that most affected pigs recover, without treatment, in a week or two.

In the early stages of the disease, even in its nonclinical form, smears may show numerous inclusions and neutrophils. Later, as healing sets in, the inclusions dwindle in number and the neutrophils are replaced by lymphocytes and monocytes. These changes are also typical of those encountered in ophthalmia of the sheep, ox, goat and fowl.

DESCRIPTION OF THE INCLUSIONS

The smears were prepared and stained according to the method I [8a] described in 1931. Inclusions vary in number from one to six or seven, or even ten, in a cell and are composed of very pleomorphic granules. Sometimes the cytoplasm of the whole cell is full of more or less evenly spaced granules. In such cases no distinct and sharply demarcated inclusion (or colony of granules) can be made out. The entire cell contains one inclusion or a number of inclusions that have apparently run together.

The granules of the inclusions are best described as elementary bodies. Colonies of initial bodies are comparatively rare and never show up as clearly and as beautifully as do those in trachoma and inclusion blenorrhea. Indeed, in this disease of pigs' eyes there is not the sharp distinction between initial and elementary bodies that is found in psittacosis and in the two ocular diseases of man. Granules are seen varying in size from the large initial bodies to the small elementary bodies. The large ones stain light blue with Giemsa stain; the smallest ones stain like specks of chromatin, and the intervening sizes are stained all the various shades of blue and purple. In trachoma and inclusion blenorrhea the initial bodies are blue, the elementary bodies stain like chromatin and intervening colors are relatively scarce.

In the human diseases the elementary granules tend to be smaller than they are in the pigs' disease. The colonies, too, frequently hug or cap the nucleus of the host cell, whereas in the case of conjunctivitis of swine this is seldom so.

It is still unknown if the inclusion in the pig has a carbohydrate matrix predominantly of glycogen, such as Rice [10] showed to be present in the trachoma inclusion. The granules are gram-negative and non-

10. Rice, C. E.: The Carbohydrate Matrix of the Epithelial-Cell Inclusion in Trachoma, Am. J. Ophth. **19**:1-8, 1936.

acid-fast and stain well with Giemsa stain but poorly with other dyes. They do not inhabit the nuclei of the epithelial cells and apparently multiply only in the cytoplasm. The nucleus and cytoplasm of an infected cell do not seem to be damaged much, if at all. As nests of parasitized cells are found together, it would appear that the organisms overflow into adjoining clean cells. Penetration of the healthy cell probably occurs through its thin margin.

The granules vary in size from 0.3 to 1.75 microns. Some larger rods show bipolar staining. Pleomorphism is marked, but most of the organisms are roughly rounded or rod shaped. Many of the latter tend to taper at the ends. Triangular and more or less square types are not uncommon. In some cells the granules are most reminiscent of boomerangs.

The organisms have not yet been cultivated artificially, and nothing is known of their mode of multiplication and of their mode of natural transmission.

COMMENT

The evidence produced in this article leads to the belief that Uhlenhuth, Böing, Haendel and others were studying not only swine fever but also a new and specific infectious conjunctivitis of pigs. The conjunctival epithelial inclusions were not connected in any way with the virus of hog cholera. Their presence in animals with cholera was purely fortuitous and due, most likely, to a fly-borne infection of the eyes of the pigs in their sties. This is all the more understandable when it is remembered that Böing transmitted the conjunctival disease after an incubation period of only seventy-two hours.

This new ocular disease of swine is in all essential respects on a par with the analogous conditions in sheep, cattle, goats and fowls. Moreover, the inclusions resemble closely the Rickettsia-like organisms always associated with conjunctivitis in these animals.

It must be understood clearly that the final proof that these ocular diseases are due to the organisms described is still awaited. But the circumstantial evidence is almost overwhelming. A certain type of conjunctivitis has now been found in five different species of domestic animals, and in each species the ocular lesions are associated with intracellular Rickettsia-like organisms. This, indeed, is remarkable.

Furthermore, the disease in sheep, with its associated parasite, has been observed not only in South Africa but in the United States,[11] France,[12] the Levant,[13] North Africa,[14] the French Congo [15] and Aus-

11. Johnson, L. V.: A Pannus-Forming Infection of Sheep Eyes, Proc. Soc. Exper. Biol. & Med. **38**:42-43, 1938.

12. Lafenêtre, H.: Existence de "Rickettsia conjunctivae" du mouton dans le midi de la France, Rev. méd. vét., Toulouse **90**:323-324, 1938.

(Footnotes continued on next page)

tralia.[16] Rickettsia has been found associated with conjunctivitis of sheep and cattle in Uruguay.[17] The disease in cattle, with its associated inclusions, has been diagnosed in South Africa, France [18] and North Africa.[19] The disease in pigs, with its associated organism, has been found in Germany and in the United States. Finally, the incubation period of the disease is identical with that of the organism in all successful transmissions. All these facts tend to prove that the parasites are responsible for the ocular diseases.

This group of organisms in the domestic animals is most interesting. It seems to fill the gap between the Rickettsias of typhus, Rocky Mountain spotted fever, Mediterranean fever and tsutsugamushi disease, on the one hand, and Rickettsia ruminantium, Rickettsia canis, Rickettsia bovis, Rickettsia ovina, the L. C. L. bodies of psittacosis and the inclusions of trachoma, blenorrhoea neonatorum and Scottish tick-borne fever of sheep, on the other hand.

Leber and Prowazek created the genus Lyozoon in 1911, but the name seems to have been an unfortunate choice. Owing to the prevailing tendency to regard all organisms, such as those described in this paper, as species of Rickettsia, I called the parasites in sheep's eyes, Rickettsia conjunctivae. Though the present genus, Rickettsia, will probably be ultimately replaced by at least two or three new genera, it is convenient just now to regard these conjunctival organisms as Rickettsias. The name Rickettsia conjunctivae was also unfortunately chosen, for in 1931 it was not suspected that other Rickettsias existed in the eyes of other animals. I am inclined now to suggest the following names, so as to bring some order out of chaos and serve the ends of expediency: the sheep parasite should be Rickettsia conjunctivae ovis, Coles 1931; the goat parasite, Rickettsia conjunctivae caprae, Coles

13. Pigoury, L.: Existence de Rickettsia conjunctivae du mouton au Levant, Bull. Soc. path. exot. **30**:621-624, 1937.

14. Donatien, A., and Lestoquard, F.: Existence de Rickettsia conjunctivae du mouton, Coles 1931, en Algérie, Bull. Soc. path. exot. **30**:18-20, 1937. Cordier, G., and Ménager, J.: Existence de Rickettsia conjunctivae du Mouton, Coles 1931, en Tunisie, Bull. Soc. path. exot. **30**:224-227, 1937.

15. Malbrant, R.: Existence de Rickettsia conjunctivae du Mouton au Congo français, Bull. Soc. path. exot. **32**:907-908, 1939.

16. Beveridge, W. I. B.: Personal communication to the author.

17. Viera, O., and Castelo, M.: Conjunctivitis contagiosa por Rickettsia conjunctivae en los ovinos y bovinos del Uruguay, Rev. de med. vet. **22**:30-43, 1940.

18. Rossi, P., and Destroyat, C.: Existence en france de Rickettsia conjunctivae du boeuf, Bull. Soc. path. exot. **31**:788-790, 1938.

19. Donatien, A., and Lestoquard, F.: Existence de Rickettsia conjunctivae du boeuf en Algérie, Bull. Soc. path. exot. **30**:451-452, 1937.

1935; the ox parasite, Rickettsia conjunctivae bovis, Coles 1936; the fowl parasite, Rickettsia conjunctivae galli, Coles 1940, and the pig parasite, Rickettsia conjunctivae suis (Uhlenhuth and Böing 1910).

SUMMARY

The conjunctival epithelial inclusions associated with swine fever have been redescribed. Evidence has been adduced to show that they have nothing to do with hog cholera but probably constitute the cause of a specific conjunctivitis of pigs. The relation of the inclusions to various other organisms has been discussed.

Dr. E. V. Cowdry, of the medical school of Washington University, gave valuable assistance. Dr. P. Thygeson, formerly of Iowa State University and now of Columbia University, gave me excellent smears containing the inclusions of blenorrhea neonatorum. Mr. T. Meyer, of the Veterinary Research Institute, Onderstepoort, South Africa, prepared all the photomicrographs.

ROLE OF ANOXIA IN THE PRODUCTION OF EPISCLERITIS AND SCLERITIS

TREATMENT WITH VASODILATORS

WALTER F. DUGGAN, M.D.
UTICA, N. Y.

The cause of acute "inflammations" of the sclera is still a debatable subject, and the treatment is empiric, nonspecific, prolonged and often unsuccessful.

In Duke-Elder's textbook[1] nine and one-half pages of print suffice to describe the nonpyogenic inflammations of the sclera. He has classified them into episcleritis (nodular episcleritis and episcleritis periodica fugax) and scleritis (anterior scleritis, brawny scleritis, sclerokeratitis and posterior scleritis or sclerotenonitis). These different types shade imperceptibly into one another both clinically and pathologically, without any accurate line of demarcation. All types may be complicated by sclerosing keratitis, uveitis or both. Suggested etiologic factors include gout, rheumatism, tuberculosis, allergy, focal infection and menstruation.

PATHOLOGIC PICTURE

Duke-Elder stated:

> The lesion is characterized especially by the presence of mononuclear lymphocytes, tightly packed masses of which make up the bulk of the inflammatory nodules or the areas of diffuse swelling. . . . In the superficial episcleral lesions the conjunctiva is infiltrated in its subepithelial layers, as well as the superficial parts of the sclera, the laminae of which are separated by edema and surrounded by rows or spindle-shaped masses of lymphocytes. In these lesions extreme vascular engorgement and lymphatic dilatation occur almost invariably (Schirmer, 1895; Uhthoff, 1900). In the deeper lesions the same infiltration occurs, insinuating itself between the swollen and edematous lamellae and sometimes associated with an increase in blood vessels which become dilated and are surrounded by lymphocytes (Kostenitsch, 1894). . . . In the milder cases the inflammatory exudation may disappear leaving little or no trace; but in most cases of any degree of severity necrosis of the cells and fibers results while the new vessels undergo an obliterating endarteritis, or alternately fatty or hyaline degeneration may ensue. The necrotic tissue is then slowly absorbed; and as a rule proliferation of new fibrous tissue replaces the atrophy, leaving as the usual end-result a scar where the sclera is thinner than normal and where it may eventually become ectatic.

1. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, pp. 2044-2069.

Friedenwald,[2] after noting that scleritis and episcleritis in a certain number of cases are due to tuberculosis or to syphilis, stated: "The etiology of the remainder seem to be related to that of the non-specific inflammations of the iris, ciliary body and choroid. . . . The histological picture presented by all of these cases consists of a necrosis of some of the scleral fibres with surrounding edema and round cell infiltration."

It is apparent that the various clinical types of scleral lesions differ in degree rather than in kind and that the same type of lesion may differ from case to case in the extent and the severity of the lesion. According to this point of view necroscleritis nodosa is the extreme stage of a nonpyogenic focal scleral inflammation.

Except in the cases of episcleritis periodica fugax and anterior scleritis, both of which often occur in young adults, most of the scleral "inflammations" occur in the older age groups. Many of these clinical types are chronic, recurrent, protracted and resistant to treatment. Enucleation is not an uncommon sequela.

TREATMENT

In the past the treatment of scleral and episcleral "inflammations" has been nonspecific, varied and not too successful. General treatment has included injections of tuberculin for tuberculin-sensitive patients, elimination of foci of infection, elimination of allergins, administration of vaccines, salicylates and iodides, injections of milk and autohemotherapy. Local treatment has included the use of leeches, hot compresses, yellow oxide of mercury ointment, radium and, in some cases, mydriatics.

PATHOLOGIC PHYSIOLOGY

It must be apparent that the early changes in episcleritis and scleritis are basically similar to those which occur in acute retrobulbar neuritis, acute exudative choroiditis, acute iritis, iridocyclitis, cyclitis and acute closure of the central retinal artery or one of its branches. I have recently discussed the similarities between these superficially different clinical pictures [3] and observed that the early pathologic picture can be ascribed to increased capillary permeability and arteriolar spasm, with resulting tissue anoxia. The early pathologic change consists of localized edema and round cell infiltration corresponding to Ricker's stages of prestasis and peristasis. There is also capillary and venular dilatation, and the round cell infiltration is perivascular. In cases of

2. Friedenwald, J.: The Pathology of the Eye, New York, The Macmillan Company, 1929, pp. 67-69.

3. Duggan, W. F.: The Vascular Basis of Uveal Disease: Acute Anoxia as the Fundamental Pathologic Physiology, Arch. Ophth. **24**:1123 (Dec.) 1940.

severe involvement in which the localized anoxia is of sufficient intensity and duration, focal necroses occur. With subsidence of the lesions, development of connective tissue or glial tissue results in focal scarring.

The focal nature of these lesions must be due to a hypersensitivity of one or more arteriolar-capillary units accounting for the sharply localized lesions.

ETIOLOGY

There are probably multiple causes for the scleral "inflammations." Substances which act on the capillaries, on the arterioles or on both are possible etiologic agents.

Capillary permeability is increased beyond physiologic limits by lack of available oxygen in the circulating blood (Landis), by lack of ascorbic acid, by histamine, by certain drugs and by spasm of the arterioles supplying the involved capillaries.

Arteriolar spasm can be caused by overaction of the sympathetic nervous system, by an increase of epinephrine in the circulating blood, by nicotine, by histamine or histamine-like bodies and by a decreased formation or an increased destruction of acetylcholine, the vasodilator hormone of the body.

Lack of histaminase may play a role in the cases in which the condition can be attributed to histamine. However, since histaminase is presumed to act by aiding in the oxidative removal of histamine, since commercial histaminase is a tissue extract and since many tissue extracts have arteriolodilating properties, it is not unlikely that histaminase preparations act by making oxygen-containing blood available to the capillaries as well as by neutralizing histamine.

Other factors must be considered briefly. Thiamine is said [4] to act by augmenting the action of acetylcholine; so lack of thiamine may cause arteriolar spasm. Nicotinic acid is also a vasodilator, as any one can prove to his satisfaction by taking 50 mg. with the stomach empty. Thiamine, nicotinic acid and riboflavin all seem to be concerned with oxidative processes in the body. Therefore, vascular dysfunction with resulting capillary and tissue anoxia may be the body's reaction to inadequate intake, absorption or utilization of the vitamin B complex.

In cases in which the condition is ascribed to menstruation it is said to be due to an excess or deficiency of certain hormones in the blood. Reynolds [5] has reported that estrogen is cholinergic, in that it apparently increases the acetylcholine content of rabbits' uteri. Therefore, lesions

4. Minz, B.: Le rôle de la vitamine B_1 dans la régulation humorale du système nerveux; propos thérapeutiques, Presse méd. **46**:1406 (Sept. 21) 1938.

5. Reynolds, S. R. M.: Cholinergic Action of Oestrin, Science **87**:537 (June 10) 1938.

attributed to endocrine deficiencies may be due to angiospasm resulting from failure of the hormonal mechanisms concerned with maintaining homeostasis.

Another contributing factor may be temporary alkalosis due to ingestion of alkali or to hyperpnea with a consequent "blowing off" of carbon dioxide. Physiologic anoxemia results because the dissociation curve of oxyhemoglobin is shifted to the left. In the presence of other likely etiologic factors this transient physiologic anoxemia could be of etiologic significance, as it definitely is in cases of epilepsy.

Histamine or histamine-like bodies are probably of major etiologic importance, because histamine acts on both arterioles and capillaries. A histamine origin satisfactorily explains the conditions which have been attributed to allergy and to focal infection. Moreover, the formation of histamine in the skin after exposure to cold and its transport by way of the blood to histamine-sensitive cells elsewhere in the body, as discussed by Horton, Brown and Roth,[6] adequately accounts for the occurrence of these conditions in the cold months of the year.

A histamine origin of the inflammations attributed to tuberculosis is logical, because Corelli [7] has reported that subcutaneous injections of tuberculin caused intensification of cutaneous and intradermal positive tuberculin reactions. As I have stated elsewhere,[8] "a positive tuberculin reaction . . . does not necessarily indicate a specific infection. Such positive reactions may only mean that there is histamine in the circulating blood. Therefore, in adults, these positive skin tests may actually be tests for histamine hypersensitivity." Since many of these acute scleral "inflammations" follow exposure to cold (see cases 4 and 5), an increase of histamine in the circulating blood satisfactorily accounts for them as well as for a positive tuberculin reaction.

In the final analysis all such conditions can be interpreted as manifestations of acute localized tissue anoxia due to varying degrees of arteriolar spasm and increased capillary permeability accompanied with capillary and venular dilatation. These vascular changes are the final common pathway whereby a number of different etiologic factors can produce the same clinical lesion. Many of these etiologic factors are of endogenous origin and become operative because of temporary failure of homeostatic mechanisms within the body. Probably multiple etiologic factors are operative in most cases.

Since vasodilator therapy has been of value in the treatment of other lesions attributable to vascular dysfunction, it seemed to be indicated in cases of episcleritis and scleritis. For this reason the following cases are reported.

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6. Horton, B. T.; Brown, G. E., and Roth, G. M.: Hypersensitiveness to Cold, J. A. M. A. **107**:1263 (Oct. 17) 1936.

7. Corelli, F.: Il fenomeno della "riaccensione istaminica" di manifestazione allergiche cutanee e viscerali, Policlinico (sez. med.) **44**:491 (Oct.) 1937.

REPORT OF CASES

CASE 1 (episcleritis).—W. P., a man of 58, was seen on March 24, 1938, with the complaint that on March 18 the right eye had become red and teared. Chemosis and photophobia developed on March 24. The patient had had malaria, typhoid fever and yellow fever. His upper teeth were false, and he had several rotten roots and one capped tooth in his lower jaw. There was no history of gonorrhea, syphilis or tuberculosis, and his general physical condition was otherwise good.

Vision in the right eye was 20/30—. Just behind the limbus, "between 10 and 11 o'clock," there was a typical tender purplish nodule of episcleritis. The tension, field and fundus were normal.

He was given 30 mg. of erythrityl tetranitrate U. S. P. twice daily, orally, for five days and 0.1 Gm. of sodium nitrite intravenously on March 24 and 29.

There was progressive improvement in the lesion. On March 26 the nodule had disappeared. There was no tenderness, and only a faint purplish injection and a little subconjunctival edema indicated the site of the lesion. On March 31 only a few dilated episcleral venules were present. When he was seen last, on April 12, the eye was completely white, and the vision was 20/20—.

CASE 2 (episcleritis).—W. W., a man of 30, was seen on Aug. 13, 1938, with the complaint that the right eye had been red, painful and sensitive to light for one month. He gave a history of many previous attacks of episcleral inflammation in both eyes for several years.

Vision in the right eye was 20/30. There was a typical nodule of episcleritis temporal to the limbus, with several old corneal opacities in the temporal half of the cornea.

Vision in the left eye was 20/70. Owing to repeated attacks of episcleritis, the sclera was porcelain white, and the cornea showed many opacities, the result of sclerosing keratitis.

He received five daily intravenous injections of sodium nitrite (0.1 Gm.) from August 13 to 17 inclusive, followed by 15 mg. of erythrityl tetranitrate by mouth twice a day until August 21, after which the dose was given once a day.

Improvement was slow but steady. On August 15 there was a definite improvement, and on August 17 the right eye was almost white. Symptomatic relief continued until September 3, when he was given a final injection of sodium nitrite. At his last visit, on September 7, the eye was white; the nodule had disappeared, and there was no local pain or tenderness.

CASE 3 (scleritis).—M. M., a man of 61, was seen on Sept. 23, 1938, with the complaint that the right eye had been red and painful for four days. The vision was 20/20, and there was marked injection of the lower palpebral and bulbar conjunctiva. The physician who saw him prescribed mild protein silver and hot compresses.

The patient returned on September 30, with the complaint of inability to sleep at night because of pain in the eye. At this time he showed generalized episcleral and conjunctival injection with chemosis above the cornea. The globe was tender everywhere, especially above the cornea, and he complained of severe generalized pain in the eye. The anterior chamber, iris and fundus were normal.

He was given six daily intravenous injections of sodium nitrite (0.1 Gm.) between September 30 and October 5. On October 4 he began the use of erythrityl tetranitrate, 15 mg. twice daily by mouth.

His pain was relieved after the first injection, and the tenderness was markedly decreased after the fourth injection. The episcleral congestion decreased from day to day, so that when he was last seen, on October 7, the eye was almost white and not abnormally tender. He failed to return to the clinic after this date.

CASE 4 (brawny scleritis).—Mrs. C. H., 68 years of age, was seen on Jan. 14, 1940, with the complaint that the right lids had been swollen and the right eye had been fiery red, tender, painful and tearing since awakening on January 12. She also had a severe headache. A similar condition had developed in the left eye on January 13. The only apparent cause that could be elicited was that she had been out in the cold on January 11 and 12. Several years previously she had suffered from a severe attack of rheumatism, and she still had occasional attacks of pain and tenderness in her knees.

The vision was 20/30— in the right eye and 20/20— in the left eye. The right eye showed marked chemosis and a purplish red congestion of the episcleral vessels from the limbus to the equator. The eyeball was extremely tender, especially near the insertions of the rectus muscles. There was also slight edema of the lids. The left eye showed the same changes to a slightly lesser degree.

The pupils reacted normally, and the tension, fields and fundi were normal. Incipient lens opacities were present, more marked in the right than in the left eye.

She was immediately given 0.1 Gm. of sodium nitrite intravenously and told to take 15 mg. of erythrityl tetranitrate that night.

When she returned, on January 18, she was markedly improved. The edema of the lids, chemosis, pain and tenderness were no longer present, and all of the episcleral injection had disappeared except a tiny patch nasal and temporal to each limbus. A second injection of sodium nitrite was given at this time.

On January 22 the eyes were completely white and showed no signs or symptoms of the scleritis.

CASE 5 (episcleritis).—I. S., a man of 65, was seen on Jan. 21, 1940, with the complaint that the lower portion of the left eye had been red for one week. On January 18 the inferior bulbar conjunctiva became so swollen that it protruded slightly between the closed lids, and there was pain in the eye when he looked down. The history was otherwise irrelevant except for the fact that he had spent January 15 and 16 out in the cold weather.

Vision in the left eye was 20/25—. Below the cornea there was such marked chemosis of the conjunctiva that it protruded between the closed lids. Beneath the chemotic conjunctiva one could see and feel a tender, purplish nodule of episcleritis close to the insertion of the inferior rectus muscle. The pupil dilated widely with one drop of scopolamine hydrobromide solution. The fundus was normal.

The patient was immediately given 0.1 Gm. of sodium nitrite intravenously. On the following day (January 22) the chemosis had disappeared; there was no tenderness, and only a trace of episcleral congestion was present. A second injection of sodium nitrite was given, and 30 mg. of erythrityl tetranitrate was ordered for use at night for three days.

On January 24 the eye appeared normal, and it has remained so until the present time.

In 1 case of episcleritis periodica fugax this treatment afforded dramatic relief of the pain and tenderness. The patient, a man of 36, who had had attacks for seventeen years, was extremely uncooperative in attending a clinic. He was seen on March 9, 1938, during an attack which had lasted for one week. The left eye was so tender that it was

impossible to palpate the eye for tension. Thirty minutes after an intravenous injection of sodium nitrite (0.1 Gm.) the pain had disappeared, and the patient did not complain of any pain when the eye was palpated more vigorously than is customary in determining the tension by palpation.

COMMENT

The acute "inflammations" of the sclera are similar in their early pathologic character to the acute "inflammations" of the optic nerve, choroid, iris and ciliary body and to acute closure of the central retinal artery or one of its branches. All agents which, in virtue of their presence or absence, can increase the permeability of the capillaries, cause arteriolar spasm or, like histamine, bring about both effects are possible etiologic agents.

Venous congestion due to venular and capillary dilatation and edema due to increased capillary permeability are the obvious gross changes. Edema, vascular engorgement and round cell infiltration are the outstanding microscopic observations. The pathologic physiology is tissue anoxia. If this tissue anoxia is of sufficient duration or intensity, tissue necrosis occurs; an infarct results, and the globe perforates or connective tissue ingrowth repairs the lesion.

There is as much variation among the different clinical types of acute scleral disease as there is among the many varieties of acute uveal disease. The differences seen from lesion to lesion in the same tissue are quantitative rather than qualitative. The superficial differences occurring when the same basic pathologic picture is present in different tissues are due to differences in the tissues themselves and to the modifying effect of these differences on the development of the lesion.

The pathologic picture described is that of allergy. It is also that of histamine poisoning and of shock in miniature (Moon). Allergy presupposes previous sensitization by a protein. Since one theory of allergy and anaphylaxis is known as the "histamine" theory and since, as Corelli has shown, histamine can intensify cutaneous reactions to allergens, one can logically attribute all scleral inflammations formerly ascribed to tuberculosis, allergy and focal infection to histamine.

Moreover, altered reactions of the arterioles and capillaries with resulting tissue anoxia can result from an inadequate supply of thiamine, nicotinic acid and ascorbic acid. Even the conditions ascribed to menstruation can be interpreted as of vascular origin.

Many writers have drawn an analogy between these scleral lesions and rheumatism because of the occurrence of both conditions in the same patient. However, episcleritis and scleritis are not due to rheumatism or arthritis. Both are manifestations of a similar vascular pathologic change in different tissues. It is of some interest that all patients who

have had acute rheumatic symptoms and have been treated for an angiospastic ocular lesion have also been relieved of the rheumatic symptoms after the use of vasodilators. Vasodilators seem to be as effective in the treatment of the acute nonpyogenic scleral "inflammations" as they are in the treatment of other ocular lesions which can be ascribed to acute localized tissue anoxia of vascular origin. In the 5 cases reported the time necessary for clinical cure varied between three and eight days. No therapy other than administration of vasodilators was used in any case.

Vasodilator therapy acts only by increasing the supply of oxygen-containing blood to the anoxic capillaries and tissues. Tissue anoxia is relieved; capillary permeability is decreased; absorption of the exudate occurs, and there is a return to normal anatomy and function if the tissue anoxia has not lasted too long.

Friedenwald [8] has stated: "The practice of medicine and the study of disease are two totally different matters. In the former we are faced with the necessity for immediate action based on the most likely supposition that we can deduce from our present imperfect knowledge. In the latter we can inquire at our leisure and with full complement of skepticism as to just what is and what is not proven."

This article is concerned primarily with the practice of medicine. The theory of a primary vascular origin of these lesions may be incorrect. Theories are important only as a means for correlating diseases and treatment. Other things being equal, the simplest theory is to be preferred. The theory which seems to include the greatest number of cases is also preferable to a theory which explains only a few cases. Theories based primarily on animal experimentation are not necessarily applicable to clinical disease in human beings. Such experiments give a great deal of information about what happens when animals are subjected to various experimental procedures but tell little or nothing about clinical states in human beings. Usually young healthy animals are the subjects of these experiments. Such factors as age, exposure to cold or to climatic changes, the previous state of nutrition of the animal and neurogenic influences receive little or no attention. Different species of animals react differently when anaphylactic shock is induced or attempted, yet the basic pathologic change is the same. Human beings likewise have different lesions when all known etiologic factors are the same. The basic pathologic picture is the same for acute retrobulbar neuritis, acute exudative choroiditis, acute iritis, cyclitis or iridocyclitis and for episcleritis and scleritis, but the clinical lesions are remarkably different in their gross manifestations.

8. Friedenwald,[2] p. 73-74.

Finally, the time required for cure should be considered in evaluating the results of any new therapeutic procedure. With the passage of time many lesions subside. With some types of therapy the time required for cure is as long as with no therapy, or longer. If a new therapeutic procedure does not accomplish a clinical cure in a time materially shorter than that required for a cure without any therapy or with the types of therapy in vogue it is probably of no value. For that reason the value of vasodilator therapy should be determined by (1) its effect on the signs and symptoms of the lesion and (2) the time required for clinical cure.

SUMMARY AND CONCLUSIONS

The acute nonpyogenic scleral inflammations are manifestations of acute localized tissue anoxia and are due to increased capillary permeability, arteriolar spasm or both.

The early pathologic changes are basically the same as those associated with acute retrobulbar neuritis, acute exudative choroiditis and acute uveal disease.

The vascular changes are the final common pathway whereby a number of different etiologic factors, many of endogenous origin, produce the same clinical lesion. Hypersensitive arterioles and capillaries account for the sharply localized lesions.

In the 5 cases reported, treatment with vasodilators was of value in effecting a rapid amelioration of signs and symptoms in from three to eight days. This treatment is not empiric but is based on a consideration of the pathologic physiology which caused the lesions.

All patients may not be helped by this type of therapy. However, such treatment is definitely indicated for conditions which have formerly been attributed to allergy, focal infection, exposure to cold or tuberculosis. For these conditions a primary histamine origin is worthy of consideration.

In cases in which there are obvious vitamin deficiencies or other deficiencies, patent vascular channels insure a better opportunity for these substances to be transported to the site of the lesion.

The ampules of sodium nitrite used in 3 of the cases were supplied by E. Tosse and Co.

NECROSIS OF THE CORNEA DUE TO VITAMIN A DEFICIENCY

REPORT OF A CASE

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The purpose of this report is to record a case of necrosis of the cornea due to vitamin A deficiency occurring as a result of faulty absorption of the vitamin.

REPORT OF CASE

A 23 year old white woman was admitted to the hospital because of cramping pains in the abdomen accompanied by bloody diarrhea. The past history was noncontributory except that she had drunk considerable quantities of alcoholic liquors prior to one year previously. Her illness began a year previous to admission, at which time she began to have mild abdominal pains and two to three semisolid bowel movements a day. There was no pus, blood or mucus. She was able to continue at her work, but gradually an increase in her symptoms and increasing weakness confined her to bed. In the following six months there occurred three such episodes, in each of which she was confined to bed for approximately three weeks. On two of these occasions her joints became painful, red and swollen. Two weeks before admission she suffered an attack of influenza, and one week before admission severe generalized abdominal pain again developed, cramping in nature and associated with five to ten bowel movements daily. Four days before admission her stools became blood streaked, and later she began to pass blood and mucus only.

Examination on admission revealed an extremely emaciated person in whom pathologic findings were present on examination of the skin, eyes and intestinal tract. There were numerous circular pigmented scars scattered over the extremities and the trunk. The bulbar conjunctiva was edematous and injected, and the lids were swollen. The fundi were normal. Her general condition progressed steadily downhill. The cutaneous lesions ulcerated and assumed the proportions of a true slough. The ocular status at first showed only an injection of the conjunctival vessels. There then appeared three marginal ulcers, which advanced around the limbus and finally involved the cornea from 3 to 9 o'clock over an area of 180 degrees. The cornea of the involved area became extremely thin, and Descemet's membrane was seen to bulge forward. One observer described the necrosis of the cornea "as though it melted away." Eighteen days after admission, the descemetocele was seen to be perforated, the anterior chamber was shallow and the aqueous had escaped. The tension was very low, but no prolapse of the iris occurred. Coincident with the necrosis of the cornea the general condition of the

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patient was pursuing an analogous course. Although she was receiving thiamine hydrochloride and ascorbic acid intravenously and vitamin A by mouth, she continued to lose weight and the diarrhea still persisted. Simultaneous with the collapse of the anterior chamber the general condition had become critical. At this time she was extremely cachetic. She had had a number of tonic convulsive seizures and was completely disoriented. Transfusions of large amounts of citrated blood were given repeatedly. The vitamin A level in the blood was still below normal.[1] It had been known that patients suffering from celiac disease,[2] pancreatic disease,[3] hepatic disease [4] and dysentery failed to utilize vitamin A even though it was given in large amounts by mouth. Therefore, it was suggested that in this case the vitamin was not being absorbed and that it should be given intramuscularly.[5] The patient was given 100,000 units of vitamin A intramuscularly on three successive days. On the third day the eyes had cleared remarkably. There was beginning vascularization of the corneal defect. There was still a large ulcerated area at the limbus, but this was covered with epithelium and did not stain with fluorescein. The anterior chamber had reformed and the folds in Descemet's membrane had nearly disappeared forty-eight hours after the collapse of the anterior chamber. Within one week the corneal defect had filled in with scar tissue and the vision had become normal. The level of vitamin A in the blood had nearly doubled. The cutaneous lesions had become superficial and were granulating. There were no longer any joint pains, abdominal cramps or diarrhea. Her general condition had improved so rapidly that within three weeks the patient was discharged from the hospital. Cultures taken on aerobic and anaerobic mediums were negative for bacteria and fungi. The microscopic examination of the necrotic tissue removed from the corneal ulcers showed no bacteria but revealed only strands of necrotic tissue characterized by degenerated epithelial cells. The blood was normal except for leukocytosis (15,000 leukocytes per hundred cubic centimeters). Roentgen ray examination showed extreme ulcerative colitis that extended from the cecum to the sigmoid and was characterized by decided irregularity in outline and complete loss of normal mucosal pattern.

Xerophthalmia has been known from early times.[6] As early as 1500 B. C. it was known that patients who suffered from night blindness were cured by the inclusion of liver in the diet. From 1850 to 1900 the relation of xerophthalmia to dietary insufficiencies was frequently mentioned in the medical reports. In 1909 in animals placed on restricted diets similar ocular lesions, called ophthalmia, developed. The relation of human xerophthalmia to the condition in animals resulting from experimentation was suggested. In 1912 the absence of vitamin A was

1. Dann, W. J., and Evelyn, K. A.: Blood Levels of Vitamin A, Biochem. J. **32**:1008, 1938.

2. Breese, B. B., and McCoord, A. B.: Vitamin A Absorption in Celiac Disease, J. Pediat. **15**:183, 1939.

3. Gamble, R.: Keratomalacia and Cystic Fibrosis of the Pancreas, Am. J. Ophth. **22**:917, 1939.

4. Owen, H. B., and Hennessey, R. S. F.: Keratomalacia in Liver Disease, Tr. Roy. Soc. Trop. Med. & Hyg. **25**:367, 1932.

5. Wolff, H.: Kératite ulcéreuse et avitaminose A, Acta ophth. **16**:323, 1938.

6. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, vol. 2, p. 1753.

definitely proved to be the cause of xerophthalmia. The disease has been called xerosis from the Greek word "to dry." Actually, it is a degenerative condition characterized by dryness of the conjunctiva, due not to a diminution in the lacrimal secretion but to a change in the tissues themselves. It tends to occur in epidemic form. Blegvad [7] in 1924 reported a series of 450 cases which occurred after the first World War. In normal times the condition is seen most frequently in children who after breast feeding is discontinued become ill nourished and marasmic. In adults it occurs after a debilitating disease, especially one in which the intestinal tract is involved.

The pathogenesis of the disease is not known. Numerous investigators have shown that the prolonged absence of certain vitamins from the diet will lead to definite pathologic changes.[8] In 1921 Osborne and Mendel,[9] experimenting with animals on vitamin-A-deficient diets, observed a group of symptoms beginning with lacrimation, discharge, photophobia and swelling of the margins of the eyelids. These symptoms were not affected by the usual antiseptic procedures but did disappear if the animals were fed on a diet containing vitamin A. This work was substantiated by other workers. Mori [10] found that in animals fed on vitamin A–deficient diets the lacrimal gland showed the most striking changes. He demonstrated a shrinkage of the secretory cells. The nuclei became irregular and the cytoplasm stained poorly. Mori considered the changes of the lacrimal gland the most important in the pathologic picture, and to these changes he attributed the lesions found in the conjunctiva and cornea. Yudkin and Lambert [11] in 1923 and Mellanby and Green [12] in 1928 mentioned the antiinfective concept of vitamin A. Animals fed on a diet rich in other food products but lacking in vitamin A died as a result of an infection, most frequently from bronchopneumonia. If vitamin A or carotene was fed to the animals, the infection was prevented.

It has been demonstrated that in association with xerophthalmia there occurred degenerative changes in the myelin sheath of the trigeminal nerve. In severe cases typical wallerian degeneration occurred.

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7. Blegvad, O.: Xerophthalmia, Keratomalacia and Xerosis Conjunctivae, Am. J. Ophth. **7**:89, 1924.

8. Tassman, I. S.: Dietary Deficiency and Ocular Disease, Arch. Ophth. **8**: 580 (Oct.) 1932.

9. Osborne, T. B., and Mendel, L.: Ophthalmia and Diet, J. A. M. A. **76**:905 (April 2) 1921.

10. Mori, S.: Changes in the Para-Ocular Glands Following Administration of Diets Low in Vitamin A, Bull. Johns Hopkins Hosp. **33**:357, 1922.

11. Yudkin, A. M., and Lambert, R. A.: Pathogenesis of Ocular Lesions Produced by Deficiency of Vitamin A, J. Exper. Med. **38**:17, 1923.

12. Mellanby, E., and Green, H. N.: Vitamin A as an Anti-Infective Agent, Brit. M. J. **1**:984, 1929.

Corneal sensitivity was diminished, and with the slit lamp the corneal nerves were seen to be thickened at an extremely early period of the disease. The condition is considered of neurotrophic origin. Virchow [13] as early as 1865 mentioned the neurotrophic origin of keratomalacia. He found involvement of the central nervous system in children who had keratomalacia and who died. He called the disease "encephalitis infantilis." In 1890 Cirincione published an autopsy report on an adult who had had keratomalacia. In this case definite evidence of chronic inflammation of the gasserian ganglion was found. Changes in the brain and spinal cord have been reported in animals. It is of interest to note that there was a period in which this patient was completely disoriented and that at this time she suffered a series of tonic convulsive seizures.

Pillat [14] in 1929 visited an army camp in northern China and found a number of the soldiers to be suffering from varying degrees of ocular involvement caused by vitamin A deficiency. He divided them into groups according to the various stages of the deficiency. Night blindness was present in 33 per cent of the cases.[15] He considered this the earliest stage of the disease. The condition in the next group he called xerosis epithelialis conjunctiva. This group presented four main symptoms: Bitot's spots, xerosis of large parts of the bulbar conjunctiva, loss of luster and wrinkling of the conjunctiva. Bitot's spots are triangular areas of foam cells with the base of the triangle at the limbus and the apex directed to the lids. The wrinkling of the conjunctiva represents loss of normal elasticity of the conjunctiva. It can best be seen when the eye is moved from side to side. The loss of luster can be shown by keeping the lids separated for ten seconds. The condition in the next group he called xerosis of the cornea. It may occur with conjunctival involvement or alone. There are loss of luster and reduced sensibility of the cornea. This stage rapidly progresses to the final stage in which there is true keratomalacia. This is rarely observed in adults and is most frequently found in children. At this time there are perforation and opacification of the cornea. The eye is usually lost because of secondary infection.

The treatment of the vitamin deficiency is obvious. It must be recognized that the vitamin may not be absorbed from the digestive tract, and in cases of this kind the use of the vitamin intramuscularly may produce a dramatic response.

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13. Virchow, cited by John, I.: The Disturbance of Sensibility of the Cornea and Conjunctiva in Xerosis and Keratomalacia of Adults, Arch. Ophth. **5**:374 (March) 1931.

14. Pillat, A.: Frequency of Deficiency Diseases of the Eye Due to Lack of Vitamin A in a Military Camp, Nat. M. J., China **15**:585, 1929.

15. Pillat, A.: Main Symptoms of the Eye in Vitamin A Deficiency in Adults, Nat. M. J., China **15**:614, 1929.

SUMMARY

A case of keratomalacia due to faulty absorption of the vitamin A is reported. Emphasis is laid on the necessity of recognizing that even though sufficient vitamins may be included in the diet, absorption may be faulty and that in extreme cases of this kind parenteral administration of the vitamin is indicated.

The determination of the level of vitamin A in the blood provides an objective laboratory method of determining whether vitamin A deficiency is present.

DISCUSSION

DR. KAUFMAN SCHLIVEK: I asked Dr. Goldberg to present this case because it is timely, dramatic and instructive. He has covered the literature fairly thoroughly, and from my own experience I have little to add. Many years ago I saw 2 cases of advanced keratomalacia. The patients were marasmic children, and their corneas were cloudy and there was exfoliation of the epithelium. Both of the children were blind, and both died.

The diagnosis and the result in the case presented here were reached because I had read a report of an identical case in which a cure was obtained by injections of a Swedish preparation of vitamin A.

The most striking thing in this patient was the complete necrosis of corneal tissue—it melted away without any inflammatory signs. At first there were a few noninflammatory ulcers of the conjunctiva above the cornea, and later areas of the cornea became covered with detritus. The corneas were hypesthetic. The apexes promptly broke down, and the necrosis progressed rapidly despite the fact that the usual treatment for ulcer was immediately instituted. Three ulcers formed simultaneously on the upper tarsal conjunctiva of the right eye. The condition became serious; the anterior chamber was lost, and panophthalmitis was anticipated. I was anxious about the patient and fortunately was able to contact Dr. Jacques Lewis, who was doing some research with vitamin A.

He found that even though the patient was getting 200,000 units of vitamin A by mouth daily the blood level was low. He left some ampules of vitamin A with the resident physician, and after three injections not only was the eye saved but the patient showed prompt improvement in her general condition.

Involvement of the eye occurs late in vitamin A deficiency. Clinical ocular symptoms are: (1) night blindness, (2) xerosis of the conjunctiva and corneal epithelium, (3) keratomalacia leading to corneal necrosis, hypopyon ulcer and panophthalmitis and (4) changes in the lens.

As Dr. Goldberg mentioned, several factors may be responsible for the production of vitamin deficiency diseases. This case evidently belongs to the group due to faulty absorption of the vitamin. In certain rare cases gastrointestinal disease may result in faulty absorption, as in the case of Wilbur and Eusterman, in which the diet had been sufficient but recovery from night blindness occurred only after repair of a gastrocolic fistula.

The mechanism whereby vitamin A deficiency affects the epithelium of the conjunctiva and cornea is a matter not yet settled. The most satisfactory explanation is that it is neurotrophic. As in this case, a decrease or abolition of corneal sensitivity is a frequent clinical characteristic of keratomalacia. The corneal nerves are seen by the slit lamp to be thickened at a surprisingly early stage of the disease.

Although vitamin A was one of the first, if not the first, of the vitamins to be discovered, accurate quantitative methods of analysis have been slow of development. This can be explained by the fact that although its chemical identity has been established with reasonable certainty, synthesis of the vitamin and its separation in crystalline form were accomplished only recently.

The lessons from this case are that determination of the blood level is important, and in some cases the use of vitamin A parenterally is imperative. Even in cases of deficiency due to diet recovery may be slow, weeks or months being necessary. In this case delay would have been disastrous.

Dr. Arthur Alexander Knapp: Dr. Goldberg's presentation was an interesting one, but the patient apparently had no definite signs or symptoms of vitamin A deficiency. There were no Bitot's spots or xerophthalmia present. A picture similar to that described here was found in one of the animal experiments we did in the department of pharmacology at Columbia University, where the animal had a diet deficient in vitamin A. As far as the described improvement with vitamin A is concerned, we know that vitamins A and D are interrelated and that the absorption of the vitamin D complex and its metabolism are to some extent dependent on vitamin A. The fact that the patient had arthritis also adds to the feeling that probably this was a vitamin D deficiency rather than a vitamin A deficiency. Arthritis never has been found, so far as I know, to have a basic vitamin A deficiency, but the administration of vitamin D often has been recorded to be of great benefit to these patients.

Dr. Herman K. Goldberg: As to the arthritis, I do not think any specific vitamin is necessarily involved. It is well known that arthritis and ulcerative colitis are frequently associated. As to whether the ocular lesion was due to a deficiency of vitamin A or D, I can say only that the blood vitamin A level was extremely low. And this, associated with the dramatic response to vitamin A therapy, certainly suggests a deficiency of vitamin A.

VISUAL FIELD DEFECTS ASSOCIATED WITH CEREBELLAR TUMORS

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For the purposes of focal neurologic diagnosis, it is generally accepted that defects in the visual field indicate direct involvement of the visual pathways at some point. This is thought to be so true and so dependable that intracranial operations are often planned and performed solely on the information obtained by examination of the visual fields. The great value of perimetric examination has been repeatedly stressed by neurologic and ophthalmologic writers.

Little, however, has been written on the false clues occasionally furnished by visual field defects, or, to state it more precisely, by the field defects resulting from the effects of distant lesions on the visual pathways. In a recent survey of 158 verified tumors of the cerebellum a group of cases was encountered in which striking defects in the visual fields were found. In most of the cases they appeared so significant that the diagnoses were confused and it was necessary to rely on pneumographic studies to establish the correct sites of the tumors.

According to the literature, such circumstances must be rare, for Best,[1] writing in "Kurzes Handbuch der Ophthalmologie," declared that hemianopia is absent in cases of tumors of the cerebellum. He excepted, however, the single instance, reported by Krause, in which hemianopia was observed in a case of cerebellar tumor. This was supposedly produced by upward pressure of the tentorium against the occipital lobe. While cerebellar tumors associated with severe visual loss owing to long-continued papilledema are commonly observed, examination of the visual fields in the vast majority of cases shows only a general concentric contraction. This contraction proceeds until central vision is involved and blindness ensues.[2]

From the Department of Neurologic Surgery, Hospital of the University of Pennsylvania.

1. Best, E.: Die Augenveränderungen bei den organischen nichtentzündlichen Erkrankungen des Zentralnervensystems, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 6, pp. 513-518.

2. Rea, R. L.: Neuro-Ophthalmology, St. Louis, C. V. Mosby Company, 1938.

Cushing and Walker,[3] in an early paper, discussed the occurrence of binasal hemianopia associated with cerebellar tumors. This was said to result from the distended third ventricle pushing the optic nerves laterally against the carotid arteries so that the outer parts of the nerves were indented. It is with the hope of drawing attention to the possibilities of distant lesions producing a variety of visual field alterations ordinarily thought to result from direct involvement of the visual pathways that the following cases are recorded. They are abbreviated to the essential details.

GROUP I. HOMONYMOUS HEMIANOPIC DEFECTS

CASE 1.—The patient was a 54 year old man referred to the Hospital of the University of Pennsylvania by Dr. S. B. Molyneaux, Binghamton, N. Y. A year before admission he noted a dull ache in the back of his neck. This became increasingly more severe. Four months before admission his gait became unsteady. Irritability, failing memory and drowsiness then became outstanding complaints.

The neurologic examination was inconclusive as to localizing information. There were marked mental disturbances and questionable aphasic manifestations. Roentgen examination of the skull showed the pineal body calcified and in the midline. The optic disks were normal except for the presence of a small flame-shaped hemorrhagic deposit in the right retina. The visual acuity seemed normal to the examiner, although no visual notations were made. Perimetric examination revealed right homonymous hemianopia (fig. 1).

Although the available evidence pointed to a left hemispheric lesion, most likely either in the occipital or in the temporal lobe, the lack of evidences of increased intracranial pressure made pneumographic studies necessary for precise diagnosis. A ventriculogram was taken and showed marked symmetric dilatation of the ventricular system. In view of this, a suboccipital craniectomy was performed. A cystic hemangioma was found in the left cerebellar lobe. At autopsy a marked degree of hydrocephalus, exclusive of the fourth ventricle, was seen.

CASE 2.—The patient was a 41 year old man referred to the Hospital of the University of Pennsylvania by Dr. Samuel S. Winter of Taylor, Pa. Fourteen months before admission he began to complain of frontal headaches and dizzy spells. Shortly afterward he noted that his gait was unsteady and that there was weakness of his left leg. For three months before admission he experienced a rumbling tinnitus in his left ear. He also complained of numbness and tingling of the entire right side of his body.

He was attentive and cooperative during examination. His speech was slurred. There was marked incoordination of his left extremities, associated with considerable motor weakness. Nystagmus was present in all directions of gaze.

There was bilateral papilledema, and visual acuity was 6/22 in either eye. Examination of the visual fields demonstrated the presence of right homonymous hemianopia (fig. 1). On the basis of the clinical examination most observers thought that he had a lesion of the occipital lobe. This opinion was based on the right homonymous hemianopia. Owing to the confusing signs, a ventriculographic examination was thought necessary. This was fortunately performed and showed a marked symmetric dilatation of the ventricular system. A sub-

3. Cushing, H., and Walker, C. B.: Distortions of the Visual Fields in Cases of Brain Tumor, Binasal Hemianopia, Arch. Ophth. **41**:559, 1912.

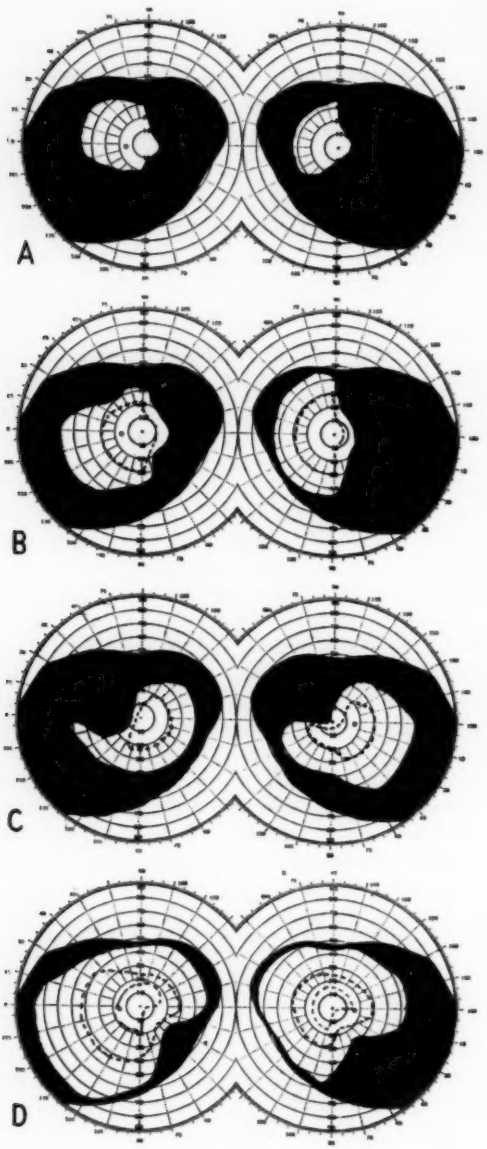

Fig. 1.—*A*, visual fields in case 1. Vision in both eyes was (questionably) normal. The perimeter test object used was the 2 mm. white. *B*, visual fields in case 2. Vision in both eyes was 6/22. The perimeter test object used was the 2 mm. red and white. *C*, visual fields in case 3. Vision in the left eye was 6/60, and in the right, 1/120. The perimeter test object used was the 2 mm. red and white. *D*, visual fields in case 4. Vision in the left eye was 6/12 +, and in the right eye, 6/15. The perimeter test object used was the 2 mm. red and white.

All 4 patients were in the neurosurgical service.

occipital exploration was thereupon carried out, but the patient's poor condition on the operating table precluded investigation of his cerebellum. At necropsy a huge hemorrhagic cyst was found occupying the vermis and compressing the pons and the medulla. Attention was called to the marked distention of the third ventricle.

CASE 3.—The patient was a 10 year old girl referred to the Hospital of the University of Pennsylvania by Dr. Adolph Reichman of Philadelphia. She had been well until four months before admission, at which time she had attacks of headache and vomiting followed shortly by staggering and by incoordination of her upper extremities.

The essential neurologic signs were incoordination in both upper extremities, posturing of the head, generalized hypotonia and nystagmus. The Bárány examination pointed to a lesion of the cerebellum. The ocular findings, however, were unusual. There was left homonymous quadrantanopia for both forms and colors (fig. 1). Visual acuity was 6/60 in the left eye and 1/120 in the right. There was bilateral papilledema of 5 D. Although the visual field defects were inexplicable and caused considerable discussion among the staff, it was felt that she showed sufficient evidences of a cerebellar tumor to justify exploration of the posterior fossa. This was done, and a cystic astrocytoma of the right cerebellar lobe was found and removed. A year later the visual field defects were essentially the same as before operation.

CASE 4.—The patient was a 13 year old girl referred to the Hospital of the University of Pennsylvania by Dr. A. M. Ornsteen of Philadelphia. For the year previous to her admission she had manifested awkwardness of her hands, and some time later she showed unsteadiness of gait. During the month before admission she had suffered severe headaches and there had been episodes of mental confusion.

On examination the child was restless, overtalkative and somewhat dull. There were marked incoordination of all four extremities and dysarthric speech. Vision was 6/15 in each eye. The optic fundi were normal. Examination of the visual fields showed a right homonymous inferior sector defect for both forms and colors (fig. 1). While she was under observation there developed papilledema and a further loss in visual acuity. Owing to the visual field defects, the situation of the tumor was placed in doubt, and ventriculographic examination was thought necessary for localization. By some observers a tumor of the temporal lobe was suspected, but the ventriculogram showed a dilated ventricular system.

A suboccipital craniectomy was performed, and a large tumor was found in the vermis and the right cerebellar lobe.

COMMENT

In this group of cases the homonymous field defects ranged from complete hemianopia to quadrantic or sector defects. In each case the diagnosis was clouded by the presence of the field defects. In 3 instances it was necessary to subject the patient to pneumographic studies to establish the location of the tumor. In 3 cases the ventriculogram showed a markedly dilated ventricular system, and in 2 cases necropsy verified the presence of a large ventricular system. The importance of this finding in the pathogenesis of the field defects will be pointed out later.

GROUP II. BITEMPORAL VISUAL FIELD DEFECTS

CASE 5.—The patient was a 15 year old boy referred to the Hospital of the University of Pennsylvania by Dr. A. W. Fees of Spangler, Pa. Four months before admission the boy had pain localized in the back of the neck. He rapidly lost weight and strength.

On examination the boy showed a slight left hemiparesis and a moderate degree of incoordination of the left extremities. Central weakness of the left facial nerve was also present. Bilateral Babinski signs were elicited. The pupils were dilated but reacted to light. There was bilateral papilledema of 4 D. Unfortunately, no notations were made of the visual acuity. Perimetric examination showed bitemporal hemianopic defects to both form and color (fig. 2). This latter finding injected so much uncertainty that ventriculographic examination was thought necessary to clarify the diagnosis. The ventriculograms showed a marked degree of internal hydrocephalus. A suboccipital craniectomy was then performed, and a large tumor was found in the left cerebellar lobe. The pathologic diagnosis was fibroblastoma.

Comment.—In this instance the diagnosis was again confused because of the visual field defects. Ventriculographic examination, which was necessary for exact diagnosis in view of the contradictory signs, again revealed a large dilated ventricular system.

GROUP III. UNCLASSIFIABLE FIELD DEFECTS

CASE 6.—The patient was a 12 year old girl referred to the Hospital of the University of Pennsylvania by Dr. Herbert Weiner of Philadelphia. Eighteen months before admission the child complained of loss of vision in the left eye. This disappeared in a few weeks, but three months later vision again became rapidly reduced in the left eye. Diplopia was complained of. A few months before admission the child complained of repeated headaches and vomiting, a buzzing tinnitus in the left ear, incoordination and staggering.

On examination it was noted that the child was obese, with the greater portion of fat distributed over the abdomen and buttocks. There was separation of the cranial suture lines as indicated by the elicitation of a cracked-pot sound on percussion of the head. There was slight weakness in the right lower extremity, and a Babinski sign was present on the right. There was staggering as well as incoordination in the upper extremities. There was no nystagmus. A marked paresis of convergence was found. The optic disks showed moderately advanced primary atrophy. Vision in the right eye was limited to the perception of hand motions and light. Vision in the left eye was 1/60. Perimetric examination showed a large central scotoma in the right eye and a small island of vision in the nasal half of the left field (fig. 2). Caloric tests gave prompt and normal reactions, except that the "shock" reactions were depressed.

On the basis of the patient's obesity, the primary optic atrophy, the loss of vision as the initial symptom and the visual field defects, the majority of observers felt that the patient had a tumor in the region of the optic chiasm. Because of the divergent neurologic signs a ventriculogram was made. This showed a tremendous dilatation of the ventricular system. A suboccipital craniectomy was then performed. A large cystic astrocytoma of the vermis was removed.

CASE 7.—The patient was a 24 year old man who was well until eight months before his admission to the hospital. At this time he had severe frontal head-

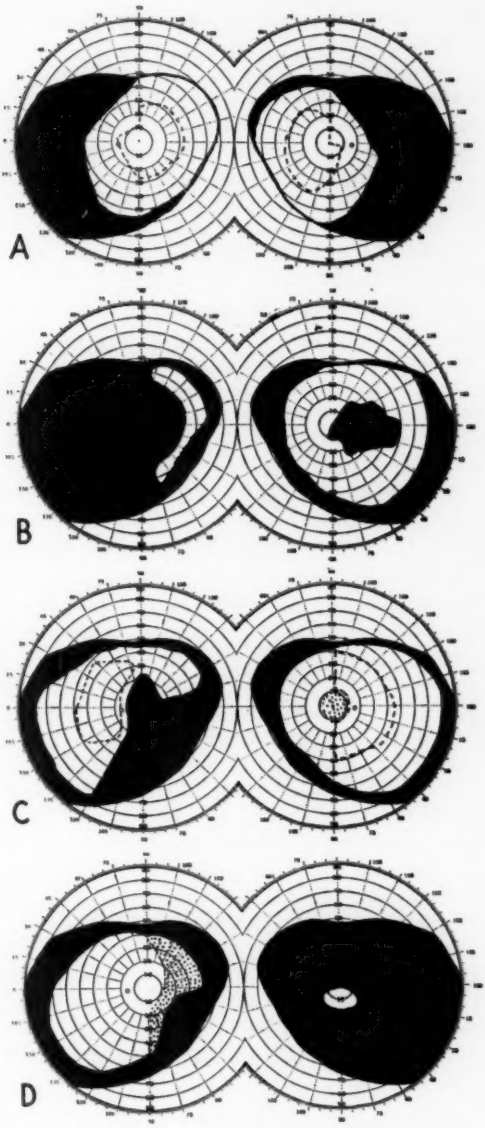

Fig. 2.—*A*, visual fields in case 5. Visual acuity was not recorded. The perimeter test object used was the 2 mm. red and white. *B*, visual fields in case 6. Vision in the left eye was limited to hand motions; in the right eye it was 6/60. The perimeter test object used was the 2 mm. white. *C*, visual fields in case 7. Visual acuity in the left eye was limited to hand motions; with the right eye the patient could count fingers at 1 foot (30.4 cm.). The perimeter test object used was the 2 mm. red and white. *D*, visual fields in case 8. Vision in the left eye was 6/60; in the right it was limited to hand motions. The perimeter test object used was the 2 mm. red and white.

All 4 patients were in the neurosurgical service.

aches and attacks of vomiting. These were followed by diplopia and failing vision. Unsteadiness in walking gradually developed, and he complained of bilateral tinnitus.

Neurologic examination revealed a moderate degree of incoordination in the left extremities and a staggering gait. There were marked endocrine disturbances, characterized by scantiness of hair, obesity, a feminine escutcheon and loss of libido. Roentgen examination of the skull showed atrophy of the dorsum sellae and evidences of increased intracranial pressure. The Bárány examination pointed to a supratentorial lesion in the midline. There was horizontal nystagmus. The fundi showed a papilledema of 4 D.; visual acuity was markedly reduced, the patient being just able to count fingers. The perimetric examination demonstrated a large inferior nasal defect in the left eye, encroaching on the macula. In the right eye there was nasal hemianopia to color (fig. 2).

The visual field defects, taken together with the evidences of destruction of the sella turcica, the clinical evidence of dysendocrinism and the Bárány report, pointed to the presence of a suprasellar tumor. The papilledema was thought due to block of the foramens of Monro. Ventricular estimation was fortunately done as a preliminary to operation, and marked dilatation of both lateral ventricles was found. The dye injected into one ventricle was quickly recovered from the other. Although considerable uncertainty as to the diagnosis was still present, a suboccipital craniectomy was performed. A cystic hemangioma of the left cerebellar lobe was found and removed.

Case 8.—The patient was a 13 year old boy referred to the Hospital of the University of Pennsylvania by Dr. H. L. Harvey of Atlantic City. The child was well until four months before admission, at which time headaches, vomiting and attacks of blurred vision set in. Soon afterward, difficulties with gait and clumsiness of the upper extremities were noticed. Shortly before admission, periods of somnolence occurred and his vision became very poor.

The essential neurologic signs were incoordination in all extremities, impaired hearing in the left ear, central weakness of the left facial nerve and paralysis of the left external rectus muscle. Nystagmus in all directions of gaze was observed. The ocular examination showed a bilateral papilledema of 4 D. Vision in the left eye was 6/60; with the right eye only hand movements were discerned. Examination of the visual fields disclosed nasal hemianopia in the left eye. Examination of the right eye with a large white object outlined a circular island of vision below the fixation point (fig. 2).

Although the visual field defects could not be explained at the time, the diagnosis of tumor of the posterior fossa seemed clear. A suboccipital craniectomy was performed, and a large medulloblastoma of the vermis was partly removed. Five months later death occurred, and necropsy showed a high degree of internal hydrocephalus.

Comment.—In addition to "atypical" field defects, in case 6 there was primary optic atrophy. This is a combination generally accepted as pathognomonic of parachiasmal lesions. Had ventriculographic examination not been performed, an incorrect operation would have resulted. In case 7 pneumographic studies were also necessary because of the diagnostic uncertainty introduced by the results of the perimetric examination. In cases 6 and 7 ventricular dilatation was noted on ventriculographic study, and in case 8 hydrocephalus was disclosed at autopsy.

GENERAL COMMENT

The characteristic sequel from obstruction of the cerebral aqueduct or fourth ventricle, occurring sooner or later with cerebellar tumors, is ventricular dilatation. If the patient survives long enough, internal hydrocephalus invariably occurs. While this fact has, curiously, not been stressed as regards the production of ocular symptoms, it has been known for several centuries that hydrocephalus may give rise to visual field defects. Gowers cited Cheselden,[4] circa 1730 or 1740, as stating that bitemporal hemianopia may result from a distended third ventricle compressing the optic chiasm. Gowers himself was well aware of this complication. Oppenheim [5] mentioned that he has seen the middle portion of the optic chiasm so compressed by a bulging third ventricle

Fig. 3.—Figure adapted from the specimen, showing an enlarged third ventricle producing compression.

that in one case "only two thin threadlike processes showed the course of the optic nerves." He mentioned in passing that cerebellar tumors may produce ventricular distention and so be the cause of bitemporal hemianopia. Wohlwill [6] also stated that in the presence of hydrocephalus the protruding third ventricle may compress the chiasm against the sella and produce bitemporal hemianopia or simple optic atrophy (fig. 3). Occasionally, he said, a diagnosis of pituitary tumor may

4. Cheselden, cited by Gowers, W. R.: A Manual of Diseases of the Nervous System, ed. 2, London, J. & A. Churchill, 1893, vol. 2, p. 144.

5. Oppenheim, H.: Textbook of Nervous Diseases for Physicians and Students, translated by A. Bruce, Edinburgh, O. Schulze & Co. [etc.], 1911, vol. 2, p. 912.

6. Wohlwill, F.: Die pathologische Anatomie der Hirnbasis, in Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1931, vol. 6, pp. 36-39.

be made. Cushing and Walker [3] cited a case of distended third ventricle resulting from a blocked cerebral aqueduct which produced a combination of optic atrophy and bitemporal hemianopia.

Since internal hydrocephalus and a distended third ventricle eventually accompany all cerebellar tumors, one can see that, theoretically at least, evidences of chiasmal compression should be frequently noted. This would be true, however, only if the anatomic relation between the third ventricle and the chiasm were constant. This is not the case. As Schaeffer [7] showed in his fundamental anatomic researches on the optic chiasm, this structure is not always in the same position. In 9 per cent of the cadavers examined the chiasm was situated completely anterior or posterior to the sella turcica. While 79 per cent of chiasms were located in some vertical relation to the chiasm, in only 12 per cent of the bodies examined was the chiasm exactly above the sella as depicted in the standard textbooks on anatomy. These normal variations in the position of the chiasm may result in many different anatomic relations with the third ventricle if it distends downward and forward. It is possible for a very large third ventricle to miss the chiasm completely, protruding between the limbs of either the optic nerves or the tracts.

There are, therefore, theoretically many possible variations in visual field defects, depending on the relation of the chiasm to the third ventricle and on the degree of ventricular dilatation. If the third ventricle compresses the chiasm, secondary complicating effects are possible because of the arteries that surround the chiasm. As has been mentioned, Cushing and Walker pointed out that arterial notching of the lateral aspects of the optic nerves may occur if the chiasm is separated by a distended third ventricle.

De Schweinitz,[8] in his classic Bowman Lecture, devoted a section to the anomalies of the arteries comprising the circle of Willis. He wrote at some length describing how indentations of the optic nerves and chiasm can be produced by these vessels if the chiasm is dislocated. The posterior communicating artery runs beneath the optic tract. In a number of dissections the vessel arose directly from the internal carotid artery, and in these instances an S-shaped curve was formed beneath the optic tract. Figure 4, which shows the relation of the posterior communicating artery to the underside of the optic tract, makes it clear how a distended third ventricle pushing the optic chiasm downward can

7. Schaeffer, J. P.: Some Points in the Regional Anatomy of the Optic Pathways, with Especial Reference to Tumors of the Hypophysis and Resulting Ocular Changes, Anat. Rec. **28**:243, 1924.

8. De Schweinitz, G. E.: Concerning Certain Ocular Aspects of Pituitary Body Disorders Mainly Exclusive of the Usual Central and Peripheral Hemianopic Field Defects, Tr. Ophth. Soc. U. Kingdom **43**:12, 1923.

stretch an optic tract over the posterior communicating artery to produce homonymous hemianopia. Though direct proof is lacking in the cases reported here, the presence of homonymous hemianopia must be explained on some such basis, since it is unlikely that a downward compression by the dilated third ventricle could in itself cause such a field defect. It is probable that arterial notchings due to dislocations of the optic nerves and chiasm against the vessels of the circle of Willis play an important role in the production of all but the bitemporal defects.

However satisfying anatomic explanations may be, they probably do not tell the whole story. It is a common experience of those seeing large numbers of adenomas of the pituitary to find that central scotomas and various bizarre combinations of field defects may occur in instances in which operation discloses the adenoma apparently pressing directly

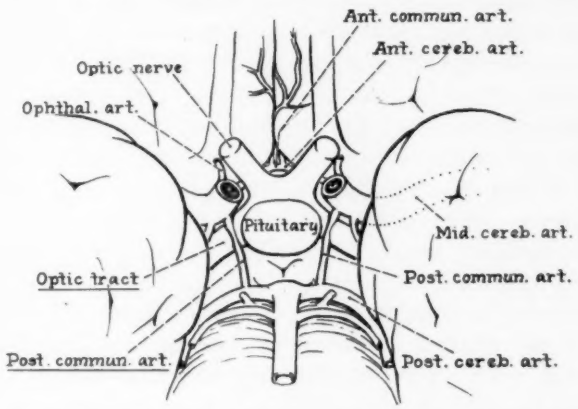

Fig. 4.—Figure adapted from the specimen, showing the relation of the posterior communicating artery to the underside of the optic tract causing compression.

upward against the optic chiasm. Whether pressure, traction or circulatory disturbance is responsible for these defects is still a question. However, with a downward-pressing mass, such as is represented by a highly distended third ventricle, the same bizarre field defects may result and the same questions arise as to the exact mechanism of production. These questions cannot, of course, be answered here; it is largely our purpose to point out that clinically the visual pathways may be affected by remote lesions in such a way as to make it appear that the optic nerves or the optic chiasm has been directly injured by a juxtaposed tumor.

In every case in which ventricular studies were performed or in which necropsy was permitted, distention of the third ventricle was apparent. Attention has been repeatedly directed to this fact during the discussion of the cases, since there is excellent ground for believing

that this is the primary mechanism in the production of visual field defects in cases of cerebellar tumors. Another additional bit of evidence that this mechanism was at work was the finding of primary optic atrophy in case 6 associated with marked "atypical" field defects. The primary optic atrophy was clearly due in this instance to direct chiasmal compression by the third ventricle.

SUMMARY AND CONCLUSIONS

Although it is generally believed that visual field defects indicate direct involvement of the optic pathways by the responsible lesions and that visual field defects therefore point to the location of the lesion, 8 cases are cited in which various combinations of field defects existed, due to verified cerebellar tumors. In 4 cases there were homonymous defects; in 2 these were homonymous hemianopias. In 1 there was a bitemporal defect, and in 4 there were various combinations of visual field defects loosely classified as "atypical." In all but 1 case the diagnosis was confused by these findings and ventriculographic studies were relied on to clarify the diagnosis. In the cases in which ventriculograms were made or autopsy was performed, a marked degree of ventricular distention was found. The third ventricle shared in the general dilatation of the ventricular system.

Though cerebellar tumors are thought not to produce field defects, it has been recognized by many writers that such defects may occur with internal hydrocephalus. Yet every cerebellar tumor eventually results in hydrocephalus. Our clinical evidence also points to the distention of the third ventricle resulting from cerebellar tumors as the primary cause for the field defects reported in our 8 cases. While direct compression of the optic chiasm may give rise to bitemporal hemianopia, the other defects, such as binasal hemianopia, homonymous hemianopia and various unclassified defects, probably depend on notching of the optic nerves and chiasm by the adjacent arteries plus the fact that the chiasm is not always in direct vertical relation with the third ventricle. Thus many and varied combinations of visual field defects may follow dilatation of the third ventricle. As a corollary point, the presence of a visual field defect does not exclude the presence of a cerebellar tumor.

PROBLEM OF DIABETIC RETINITIS

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The changes which appear in the retina in many cases of diabetes mellitus are known as diabetic retinitis. These consist mainly of hemorrhages and exudates. Because of the appearance of hemorrhages and exudates with arteriosclerosis of the retinal vessels, many observers question the ophthalmoscopic entity of diabetic retinitis. Some have been led to assume that the changes in the fundi are secondary to arteriosclerosis in any person suffering from diabetes mellitus. The changes are, however, so typical that any one familiar with the ophthalmoscopic picture on finding them is at once led to suspect the presence of diabetes mellitus, which on proper examination is always found. A causal connection between these retinal changes and diabetes must therefore be assumed, and the pathogenesis of these changes constitutes the problem of diabetic retinitis. In recent years a number of publications have reviewed this subject. Examples of such reviews are those by Waite and Beetham,[1] Braun,[2] vom Hofe[3] and Hanum.[4] All the possible pathogenic factors are discussed: blood sugar, ketone bodies, lipoids, blood calcium, arterial hypertension, arteriosclerosis and renal changes. Their conclusions are unsatisfactory. Waite and Beetham end their publication with the following statement:

> Deep retinal hemorrhages in diabetes multiply with age, and multiply with continued duration of diabetes out of proportion to the age factor, but they show no obvious correlation with sclerosis of retinal vessels, with vascular hypertension, with renal disorders, with insulin dosage or with blood sugar or calcium levels.

The problem of the pathogenesis of the diabetic changes in the retina is perhaps not capable of solution in the present state of knowledge, but I believe that it can be clarified and more definitely circumscribed.

OPHTHALMOSCOPIC PICTURE

The characteristic fundus changes, which are bilateral, are found in the area between the upper and the lower temporal vessels of the retina and in the region surrounding the optic nerve head. The optic disk

1. Waite, J. H., and Beetham, W. P.: The Visual Mechanism in Diabetes Mellitus, New England J. Med. **212**:367 and 429, 1935.
2. Braun, R.: Retinitis diabetica, Arch. f. Ophth. **136**:256, 1936.
3. vom Hofe, K.: Ueber Veränderungen am Augenhintergrund von Diabetikern, Arch. f. Ophth. **139**:801, 1938.
4. Hanum, S.: Diabetic Retinitis, Acta ophth., 1938, supp. 16, p. 3.

itself is normal in appearance, and, especially, there is no sign of edema or of swelling. In the areas mentioned there are characteristically present numerous hemorrhages of all sizes. Most of these are small, round and deeply situated and may extend out in the periphery. Radial and flame-shaped hemorrhages are seen in the superficial layers of the retina. Large hemorrhages and even a preretinal hemorrhage are occasionally observed. In addition to the hemorrhages, there are found numerous small exudates. These have an appearance of hardness, are sharply demarcated and are either white or yellowish white, some having a bright luster. The exudates are either discrete or confluent, forming all kinds of figures, including circinate ones. They are situated in the deeper layers of the retina behind the retinal vessels. Edema and cotton-wool patches are not part of the picture of diabetic retinitis and when present signify a complication due to vascular changes. The retinal vessels are usually normal in appearance, although in elderly persons and in those who are suffering from essential arterial hypertension signs of aging of the vessels and of arteriosclerosis may be found in addition to the characteristic hemorrhages and exudates of diabetic retinitis.

In addition to the hemorrhages and exudates, there occurs in some cases of diabetes a proliferative retinitis which differs in appearance from the proliferative retinitis following large hemorrhages into the vitreous. It is characterized by the presence of thin, delicate, veil-like connective tissue, which projects into the vitreous and contains fine small vessels in brushlike form or intertwined in various configurations. Thus, in 1 case a thin veil of tissue projected like a screen into the vitreous for about 8 diopters and contained within its meshes a fine network of vessels. Hanum's [4] article contains several excellent colored illustrations, and in Klien's [5] there are illustrations showing the development of these vessels and their connective tissue support. They may be found without massive hemorrhages into the vitreous, although such hemorrhages occasionally occur in diabetes.

The hemorrhages, the exudates and the proliferative retinitis constitute the fundus changes of diabetic retinitis. Of these, the hemorrhages are the most important and occur even without any exudates. The proliferative retinitis occurs only in a small number of cases.

PATHOLOGIC ANATOMY

Microscopically, hemorrhages are found in all layers of the retina. The exudates consist of colloid or hyaline material; lipoids and granular cells containing lipoids are also found. Arteriosclerotic changes are men-

5. Klien, B. A.: Retinitis Proliferans: Clinical and Histologic Studies, Arch. Ophth. **20**:427 (Sept.) 1938.

tioned in some of the reported cases. Unfortunately, persons with such pathologic involvements had during life an associated arterial hypertension and a clinically recognizable arteriosclerosis of the retinal vessels.

The histologic picture of the proliferative retinitis in diabetes was studied by Klien [6] in the eye of a diabetic patient 63 years old who had had a blood pressure of 210 systolic and 120 diastolic. There were found fatty degenerative changes in the retina and arteriosclerotic changes in the central artery and its branches. According to Klien:

> The lower part of the optic nerve and the adjoining retina were covered with a delicate membrane, which contained newly formed, thin-walled blood vessels in cross and longitudinal sections, some of them of large caliber. The framework of the membrane around these vessels was extremely delicate, consisting of a few fibroblasts, wandering cells and a faintly staining almost homogeneous transudate. The newly formed structures were on the inside of the internal limiting membrane.

There are, then, as the pathologic substratum of the ophthalmoscopic picture, hemorrhages, hyaline exudates, lipoid deposits and granular cells containing lipoids; in the cases in which proliferative retinitis is present there is also delicate connective tissue formation with numerous newly formed blood vessels. The hemorrhages occur more frequently than the exudates and are always found when these are present. I shall not further discuss the proliferative retinitis, as it forms a complication in only a small number of cases of diabetic retinitis.

RETINAL ARTERIOSCLEROSIS AND CHRONIC ARTERIAL HYPERTENSION IN ASSOCIATION WITH DIABETIC RETINITIS

The problem of diabetic retinitis is the problem of the pathogenesis of the hemorrhages and the exudates. Because hemorrhages and occasionally exudates occur with arteriosclerosis of the retinal vessels and in the course of chronic arterial hypertension, some investigators have assumed that the changes in the retina are primarily due either to arteriosclerosis or to a persistent arterial hypertension. However, a comparison of the ophthalmoscopic picture of diabetic retinitis with that of retinal arteriosclerosis and with that of chronic hypertension not associated with diabetes at once brings out the difference between the clinical pictures. Arteriosclerosis of the retinal vessels and the vessels of chronic hypertension are not accompanied by exudates or even by hemorrhages unless there is interference with the blood flow in some vessel in the retina. And when hemorrhages and exudates do occur, they have never the typical distribution and appearance characteristic of diabetic retinitis. Moreover, diabetes, especially in the young, is frequently unaccompanied by either chronic hypertension or arteriosclerosis. Among Hanum's 183

6. Klien,[5] p. 432.

patients [4] there were 88 with a systolic blood pressure below 160 mm. of mercury, and of these 31 had a pressure below 140 mm. Of Braun's [5] 111 patients, 43 had a pressure of 140 mm. or below, and 30 more had a pressure between 140 and 160 mm. Waite and Beetham [7] graded the arterial trees of 3,893 diabetic persons on the following basis: no sclerosis and sclerosis of grades 1, 1, 3 and 4. Figures with regard to absence of sclerosis on the basis of age groups follow:

		Patients Without Sclerosis	
Age group	No. of Patients	No.	%
Under 10	130	130	100
Between 10 and 19	464	451	97
Between 20 and 29	274	253	92
Between 30 and 39	315	153	48
Between 40 and 49	512	49	9
Between 50 and 59	1,001	6	0.6

Thus, 1,042 were without sclerosis, or 26 per cent of the 3,893 patients.

Waite and Beetham had 369 patients with diabetic retinitis whose systolic blood pressures were recorded. Of these, 54 per cent had a systolic blood pressure under 160 mm. of mercury.[8]

A factor in determining the frequency with which arteriosclerosis of the retinal vessels accompanies diabetic retinitis is the difference in interpretation of the signs of arteriosclerosis by various observers. Usually no distinction is made between the aging of the vessels and arteriosclerosis proper. Since diabetes occurs more frequently past middle age, the normal signs of aging of the vessels are often interpreted as arteriosclerosis. Also, since essential arterial hypertension occurs in middle age and past it, and since chronic hypertension hastens both the aging and the arteriosclerotic processes, it is natural that aging and sclerotic changes in the vessels of the retina are apt to be found in diabetic persons past middle age. In young persons diabetic retinitis is found without sclerotic changes in the vessels of the retina. Arteriosclerosis of the retinal vessels and chronic hypertension as essential pathogenic factors in the causation of diabetic retinitis can therefore be eliminated.

PRODUCTS OF METABOLISM IN ASSOCIATION WITH DIABETES MELLITUS

Other investigators have sought the cause of diabetic retinitis in some toxic substance, in the ketone bodies and in other products of metabolism. There is no known toxic substance which causes the retinal change in diabetes. Products of metabolism as pathogenic factors

7. Waite and Beetham,[1] p. 435.

8. Waite and Beetham,[1] p. 436.

have been thoroughly discussed by the authors mentioned at the beginning of this paper. The evidence so far adduced does not favor the hypothesis that products of metabolism are concerned in the production of the changes in the retina. The one other factor concerned is the persistent hyperglycemia itself which constitutes diabetes mellitus. This will be discussed later.

RETINAL CHANGES IN DIABETES AS THE RESULT OF LOCAL CIRCULATORY DISTURBANCES

It is possible to delimit the problem of diabetic retinitis more sharply by viewing the retinal changes in diabetes as the result of local circulatory disturbances there. In a previous publication [9] I discussed the mechanism of local circulatory disturbances in an organ generally and in the retina when these disturbances occur there secondary to arteriosclerosis of the retinal vessels and in the course of essential hypertension. Briefly, local circulatory disturbances occur in an organ as a consequence of interference with the blood flow through the vessels of the organ. Such interference results in various degrees of dilatation of the terminal vessel units, the prearterioles, capillaries and postcapillary venules, with a slowing of the blood flow through them producing conditions which in Ricker's terminology are known as peristasis and prestasis; or there is complete ischemia with its consequences. Peritasis is characterized by the transudation of plasma into the surrounding tissue and prestasis by the passage of red blood corpuscles, thus producing either edema or hemorrhages or both, depending on the degree of dilatation of the terminal vessel units. Hemorrhage as a result of local circulatory disturbances always occurs by diapedesis through the capillary wall when the blood flow is in a condition of prestasis. With the removal of the interference with the local circulation the fluid in the tissues returns to the blood stream, and small hemorrhages are gradually absorbed. When the dilatation of the terminal vessels persists, the slowing of the blood flow also persists; the surrounding tissue remains in a chronic state of subnutrition and of deficient oxygen supply, and secondary changes occur. The latter manifest themselves in the appearance of hyaline deposits and stainable fats and lipoids. The appearance of hyaline and of fats and lipoids where they are ordinarily not visible is always the expression of a chronically deficient oxygen supply.

The retinitis of diabetes consists of hemorrhages and of hyaline and lipoid deposits. In view of the foregoing facts, the hemorrhages in the retina must be considered as the result of prestasis, that is, as a result of slowing of the blood flow through dilated terminal vessel units. The

9. Elwyn, H.: Circulatory Disturbances in the Retina in Arteriosclerosis and in Essential Hypertension, Arch. Ophth. **21**:775 (May) 1939.

hyaline and lipoid deposits must be considered as due to the chronic state of subnutrition and chronically deficient oxygen supply secondary to the persistent slowing of the blood flow. There is no doubt in my mind that this is the correct explanation for the appearance of the hemorrhages and exudates in diabetes.

The problem of diabetic retinitis thus becomes limited to the following: There occurs in diabetes a persistent dilatation of the terminal vessel units in the retina which results in repeated hemorrhages, and as a further consequence in the appearance of hyaline and lipoid deposits there. What, then, is responsible for the dilatation of the terminal vascular elements in the retina? This is the essential problem of the retinitis in diabetes. An answer to this question is perhaps not possible at the present time. However, a tentative suggestion in the direction in which the answer must lie may be submitted. It is of interest in this connection that dilated small vessels are frequently seen in the cheeks of diabetic patients, and experienced clinicians are often able to make the diagnosis of diabetes by looking at the face of the patient.

Before a tentative answer to the question as to what causes the dilatation of terminal vessel units is offered, it is necessary to review briefly the manner in which the diabetic person differs from the normal person. In comparing the two it is important not to consider a person with advanced diabetes and complications but a person with mild diabetes in the early stages of the disease. It is also necessary to have a conception of what constitutes diabetes mellitus. The understanding of diabetes has been dominated too much by the so-called insular hypothesis, that is, by the assumption that the diminished production of insulin by diseased islands of Langerhans in the pancreas is responsible for the diabetes. Actually there is no proof that the islands of Langerhans are either diseased or insufficient. Warren,[10] who studied post mortem 484 pancreases, found hyalinization, hydropic degeneration, fibrosis, hypertrophy and lymphocytic infiltration in the islands of Langerhans. But, the islands in 127 of the pancreases, or 26 per cent, were normal as far as could be determined.[11] Hyalinization, which was the most frequent change, was found by Warren in 6 per cent of the pancreases of persons through 40 years of age and in 45 per cent of those of persons over 40.[12] The pathologic changes in the islands of Langerhans can therefore not be considered by themselves as a cause of diabetes. Also, insulin is found in the pancreases of persons who have died with diabetes, although the quantity is much less than that found in the normal pancreas, according to the figures cited by Wilder, Browne and Butt in

10. Warren, S.: The Pathology of Diabetes Mellitus, ed. 2, Philadelphia, Lea & Febiger, 1938.

11. Warren,[10] p. 224.

12. Warren,[10] p. 34.

their recent review.[13] There is, of course, no doubt that the insular apparatus in the pancreas forms an important link in the chain of control of carbohydrate metabolism.

In a publication on the pathogenesis of chronic simple glaucoma [14] I attempted to show that there is a group of diseases which are characterized primarily by the comparatively early loss of stability for the maintenance of a physiologic norm. In this group of diseases I included chronic simple glaucoma, essential arterial hypertension and diabetes mellitus. In each of these diseases the mechanism for the maintenance of a physiologic norm becomes unstable at a comparatively early age. In glaucoma it is the mechanism for the maintenance of the normal intraocular pressure which loses its stability; in essential arterial hypertension it is the mechanism for the maintenance of the normal blood pressure; in diabetes it is the mechanism for the maintenance of the normal sugar level in the blood. I shall briefly discuss this conception of the pathogenesis of diabetes mellitus.

MECHANISM FOR THE MAINTENANCE OF A NORMAL BLOOD SUGAR LEVEL

The blood sugar is maintained at a constant value, varying in different persons from 80 to 96 mg. per hundred cubic centimeters of blood. In each person under equal and constant conditions it is maintained within 5 mg. of its constant value. After administration of 100 Gm. of dextrose by mouth the blood sugar rises within about thirty minutes to about 140 to 200 mg. and then falls, gradually reaching a subnormal level within about one and a half hours. The mechanism which maintains the constant normal value of dextrose in the blood has not been completely clarified. The liver is definitely one of the effector organs. Central regulation in the central nervous system has been known to exist since Claude Bernard produced glycosuria by puncturing an area in the fourth ventricle. It is probable that the center of regulation for blood sugar is situated in the hypothalamus. Neural connection between the hypothalamus and the liver is known. Hormonal control is par excellence by the hormone of the islands of Langerhans in the pancreas, insulin; fibers of the vegetative nervous system are found in the pancreas. While one of the effector organs, the chief hormonal control and part of the central regulation are known, the whole mechanism is not yet clear. Yet it is obvious that a mechanism for the maintenance of a normal blood sugar level which is the optimum for the organism exists.

13. Wilder, R. M.; Browne, H. C., and Butt, H. R.: Diseases of Metabolism and Nutrition: Review of Certain Recent Contributions, Arch. Int. Med. **65**:390 (Feb.) 1940.

14. Elwyn, H.: Pathogenesis of Chronic Simple Glaucoma, Arch. Ophth. **19**: 986 (June) 1938.

MECHANISM FOR THE MAINTENANCE OF THE BLOOD SUGAR LEVEL IN CASES OF DIABETES MELLITUS

Diabetes, like essential hypertension and chronic simple glaucoma, begins in middle life, in the forties or earlier, and occasionally in a young person. In following the course of the disease several stages similar to those of the other two diseases are observed. At first there is only an exaggeration of the normal variations in the blood sugar level. The blood sugar rises higher than normal after a meal and takes longer to reach the previous level. After oral administration of 100 Gm. of dextrose, the blood sugar rises to a higher level than normally, and the higher level persists for a longer time. With the passing of time the greater variations persist and the blood sugar level is higher for longer periods. With time, the blood sugar level remains permanently high. When no treatment is given secondary changes as a result of the loss of sugar appear. This loss is accompanied by the mobilization of the glycogen stores in the liver and the conversion of glycogen into dextrose, which enters the blood stream. This loss of glycogen is harmful to the liver, for it seems that almost all of its chemical activities depend on the integrity of its glycogen function.[15]

CONCEPTION OF THE PATHOGENESIS OF DIABETES MELLITUS

I conceive diabetes mellitus to be a disease in which the mechanism for the maintenance of the normal blood sugar is inherently deficient. Instead of retaining its normal stability throughout life, it becomes unstable during middle life and occasionally in young persons. The cause of the instability is not to be found in the effector organs such as the liver, in the islands of Langerhans or in the peripheral vegetative nervous system. It is to be found in the mechanism as a whole or in its central regulation in the brain. The fault in the central regulation is not to be sought for in gross pathologic changes there but in an inherent weakness of the proper gearing of the individual parts of the mechanism. At first the instability of the mechanism is slight, resulting only in exaggerated variations of the normal fluctuations of the sugar level and of an abnormal response to tests. After a considerable period of time the instability becomes more marked, and the inability to maintain the normal blood sugar level is more outspoken.

The cause of the inherent instability is to be found in an inherited defect of the mechanism already present in the germ plasm and appearing at a definite early period in life. The factor of heredity in diabetes mellitus has been amply demonstrated.

In looking for the essential difference between the normal person and the person with mild diabetes, especially in the early stages of

15. Roger, cited by Wilder, Browne and Butt,[13] p. 394.

the disease, it is evident that this difference consists in the increased level of the blood sugar, excluding, of course, the normal rise in blood sugar level after meals. Whenever the blood sugar level remains above the allowable high limit of normal, then one has diabetes mellitus, even when the high level is far below the renal threshold for sugar elimination and even when there are no subjective symptoms. It is only in this hyperglycemia that the diabetic person differs essentially from the nondiabetic person. All the other metabolic disturbances which occur in the later stages and in the severer forms of the disease are secondary to the hyperglycemia and to the consequent loss of glycogen reserve. There is no question of the ability of the patient with diabetes, especially the mild diabetes, to utilize carbohydrates. He has no other disturbances aside from increased blood sugar level.

INCREASED BLOOD SUGAR LEVEL AS A FACTOR IN DIABETIC RETINITIS

In returning to the question as to what causes the dilatation of the terminal vessel units in the retina and the state of prestasis which is responsible for the hemorrhages and exudates, it is logical to assume that the one element which differentiates the diabetic from the nondiabetic person, the hyperglycemia, is the responsible factor. It is not necessarily the person with severe diabetes who suffers from the retinal changes but more often the person with mild diabetes who has had hyperglycemia for a long time. The persistently increased sugar level in the blood influences the terminal vessel units in some unknown manner in producing slight dilatation of these vessels in an irregular distribution through the retina. This results in a chronic state of prestasis with repeated hemorrhages into the retina and in a chronic state of subnutrition and of deficient oxygen supply with the consequent appearance of hyalin and lipoids.

CONCLUSION

Diabetic retinitis cannot be explained on the basis of retinal arteriosclerosis or chronic hypertension even when these conditions coexist. The hemorrhages and exudates which constitute diabetic retinitis can be explained as a result of local circulatory disturbances in the retina. Hemorrhages result when the terminal vessel units are in a certain definite state of dilatation, with a corresponding slowing of the blood flow—prestasis, in the terminology of Ricker. A condition of prestasis in the retina must be assumed from the presence there of the hemorrhages. When the state of prestasis persists for a given length of time, the corresponding part of the retina receives an insufficient food and oxygen supply. As a result, hyalin is deposited in the tissues of the retina, and lipoids become visible. The problem of diabetic retinitis

narrows down to the question: What is responsible for the dilatation of the terminal vessels and the state of prestasis in the retina?

A tentative suggestion may be offered. Diabetes mellitus belongs to a group of diseases which is characterized by the loss of stability of the mechanism for the maintenance of a physiologic norm. In the case of diabetes it is the mechanism which maintains the blood sugar level which is at fault. The result is an unstable and increased sugar level in the blood. All the secondary metabolic changes are due to the consequent loss of sugar with its attendant loss of glycogen reserve in the liver. The persistently increased sugar level in the blood affects the terminal vessel units in an unknown manner to cause dilatation. The resultant slowing of the blood flow constitutes the condition of prestasis with its attendant hemorrhages into the retina and is responsible for the eventual deposit of hyalin and lipoids.

Clinical Notes

AIR EMBOLI IN THE RETINAL ARTERIES

Report of a Case

ROBERT T. WONG, M.D., CLEVELAND

The visualization of air emboli in the retinal arteries has been occasionally reported. Hirsch [1] (1920) was one of the first authors to report this finding. Reyer and Kohl [2] reported the observation of bubbles of air in the retinal arteries in 1 of a series of 10 patients with gas embolism. Weaver [3] and others have described retinal changes after injection of air into the arterial systems of experimental animals. The following account of a clinical observation of the passage of bubbles of air along the retinal arteries after introduction of a large air embolus into the vascular system is given because of the rarity of this observation and because of some of the unusual, hitherto unmentioned, features observed in this case.

REPORT OF CASE

M. R., a white woman aged 24, with moderately advanced pulmonary tuberculosis, was admitted for treatment to the City Hospital June 24, 1940. On August 19, during an aspiration of the right extrapleural space for evacuation of an effusion, the patient suddenly became unconscious, rigid and cyanotic. The heart sounds could not be heard, but labored, shallow respirations continued for about seven minutes; then death occurred. Examination of the ocular fundi was begun about five minutes before respirations ceased, and observations were continued for the next fifteen minutes.

The pupils were 7 mm. in diameter and rigid to direct light stimulation. The media of the right eye were clear. The disk was white. The retina was pale; later it became cyanotic. The retinal arteries were of normal size and contour and of even caliber. Interspaced at irregular intervals between columns of blood in the arteries were pale silvery sections, varying from 1 to 4 vessel diameters in length, which appeared successively at the bifurcation of the central artery, moved forward and disappeared rapidly from view at the periphery of the main branches of the central artery. From eight to twenty bloodless sections could be seen in the field at one time. After about one minute the flow stopped; the arteries became attenuated and emptied of blood, and later they were barely visible as silvery white

From the Department of Ophthalmology of the City Hospital, Cleveland, service of Dr. Paul G. Moore.

1. Hirsch, C.: Luftembolie in Arteria centralis retinae nach Kieferhöhlenspülung, Klin. Monatsbl. f. Augenh. **75**:625, 1920.

2. Reyer, G. W., and Kohl, H. W.: Air Embolism Complicating Thoracic Surgery, J. A. M. A. **87**:1626 (Nov. 13) 1926.

3. Weaver, E.: Cerebrale Luftembolie, Beitr. z. Klin. d. Tuberk. **31**:159, 1914.

streaks. The veins were dark, dilated and engorged with blood. About five minutes after respirations ceased, the columns of blood in the veins began to break into segments. Compression of the thorax caused the sections to move slowly toward the periphery, and relaxation of pressure reversed the movement.

In the left eye the arteries were attenuated and filled with blood. No break in the blood column was seen at any time. The veins were dilated and engorged. Segmentation of the venous column occurred about the end of the observation period.

At necropsy the heart was exposed and submerged in water. Puncture of the left ventricle was followed by the escape of numerous large bubbles of air, which established the diagnosis of gas embolism in the vascular system. The eyes were not examined.

COMMENT

The slow injection of air into the right common carotid artery of an anesthetized dog produced the same changes in the ocular fundi as were observed in the right eye of the patient. It is safe to assume that the phenomenon observed in the retinal arteries was caused by bubbles of air accidentally introduced into the vascular system during the pleural aspiration.

Obituaries

BEN WITT KEY, M.D.
1883-1940

Dr. Ben Witt Key, an active member of the Section of Ophthalmology of the New York Academy of Medicine for nearly thirty years, died, after a prolonged illness, on June 5, 1940, in New York, at the age of 56.

Dr. Key was born at Cuthbert, Ga., on June 11, 1883, the son of the Rev. Benjamin Witt Key and Adelia Allen Key and grandson of Bishop Joseph S. Key of the Methodist Episcopal Church, South.

He received his B.A. degree at Vanderbilt University, where he was active in student literary affairs and a member of the baseball team. His medical education was received at the University of Pennsylvania, from which he graduated with honors in 1909. It was at the University of Pennsylvania that he came in contact with the late Dr. George de Schweinitz, whose example and good influence largely determined Dr. Key's selection of ophthalmology as a career.

Shortly after graduation Dr. Key entered the New York Eye and Ear Infirmary as an intern and was promoted steadily until he attained the rank of surgeon, in which position he served with great credit until his health failed in 1937. For the past two years his connection with that institution was as honorary surgeon.

Dr. Key practiced ophthalmology in the city of New York for over thirty years, during which period, in addition to his connections with the New York Eye and Ear Infirmary, he was attending surgeon at New York University College of Medicine and held a similar position at the French hospital.

Dr. Key was an intense and greatly interested student of ophthalmology and was a regular attendant at meetings of local and national societies and an active participant in their proceedings. He frequently contributed to ophthalmologic literature on various subjects and was one of the pioneer advocates of the use of nonspecific protein therapy in the fight against infections of the eye, publishing several papers advocating the use of antidiphtheritic serum as the most acceptable medium for this work.

He was a skilful and meticulous eye surgeon and was among the first few in this country to publish an account of a personal experience with the operation of keratoplasty by means of a human corneal transplant.

Dr. Key was a member of the American Medical Association, the New York Academy of Medicine, the Harvey Society, the American

College of Surgeons, the American Academy of Ophthalmology and Otolaryngology and the American Ophthalmological Society, in the last-named society serving for a term in the critical capacity of a member of its committee on theses.

His greatest diversion was travel, and nearly every year he devoted his vacation to this means of recreation by extensive trips either abroad or in this country. Golf was his game, and until the last few years, in spite of a busy practice, he found time to get in an occasional round on nearby courses.

In 1913 Dr. Key was married to Sarah Webb, daughter of Mr. and Mrs. John M. Webb of Bell Buckle, Tenn. His wife, his only daughter, Mrs. James Owen Watts Jr., of Lynchburg, Va., and a grandson, James Owen Watts III, survive him, as do his mother and a half-brother, Henry Clay Foster, of Englewood, N. J.

Whereas, the Section of Ophthalmology of the New York Academy of Medicine feels deeply that the death of Dr. Ben Witt Key has deprived them of one of their most respected and beloved members, be it resolved that a copy of the foregoing be spread on the minutes of this Section and furthermore that a copy be sent to his widow, Mrs. Ben Witt Key.

SAMUEL P. OAST.

EMORY HILL, M.D.
1883–1940

Emory Hill was the son of James Christian Hill and Mrs. Mary Emory Lamb Hill. He was born on Sept. 8, 1883 at Scottsville, Va., and died on Dec. 4, 1940 at Richmond, Va. He married Miss Julia Duval Hawes, of Charlottesville, Va., on April 18, 1911. He is survived by his wife, two sons, Walker Hawes Hill and James Christian Hill, and two sisters.

He received the degree of B.A., from Columbia University and, in 1907, the degree of M.D. from the Medical College of Virginia. He interned first at the Philadelphia Orthopaedic Hospital and Infirmary for Nervous Diseases, where he came under the influence of S. Weir Mitchell, Wharton Sinkler, Morris Lewis and William Hunt, physicians of outstanding eminence in the fields of neurology, internal medicine and surgery. The following year he entered Wills Hospital as an intern, and while there he published in joint authorship with his associate, Charles W. Jennings, an article on the etiology of iritis, the first paper by interns who used the case records of the hospital for statistical study. At the termination of his service he went to Chicago as personal assistant to Dr. Cassius Wescott. While in Chicago, he took graduate work at the University of Chicago and later became an instructor in ophthalmology at Rush Medical College. In 1919 he removed to Richmond, Va., and practiced ophthalmology there until his death.

In 1929 he succeeded Dr. Joseph A. White as professor of ophthalmology at his alma mater and held this position until 1938. He was much interested in the younger men, and several of his associates have gained positions of prominence in the local schools and clinics.

He was admitted to the American Ophthalmological Society in 1920 and served as secretary-treasurer of the society from 1925 to 1932.

Among the many societies of which he was a member was the College of Physicians of Philadelphia, to which he was elected because of the position he held in ophthalmology and because of his interest in the Section on Ophthalmology of the college. He was a Fellow of the American Medical Association and of the American Academy of Ophthalmology and Otolaryngology.

Although Dr. Hill did not contribute a great number of articles to the literature, those that he did publish were of considerable interest and value and were written in a clear concise style. Dr. Hill was a good teacher and gave freely of his time to various instructional courses given throughout the country. He was devoted to his work and was an intelligent observer and skilful operator.

Dr. Hill was of a generous, unselfish and kindly nature. He possessed an independent, progressive mind and when the occasion demanded

left no one in doubt as to his views on social, economic and religious subjects. He had a high sense of right and justice; indeed, it might be said of him, as was said of another, that "justice was his worship, and humanity his religion." He despised cant and sham and honored forth-

EMORY HILL, M.D.
1883-1940

rightness and genuineness. He could well have said, in the words of William Ernest Henley:

"My task accomplished; the long day done;
and my wages taken.

. . . . . .

Let me be gathered to the quiet West,
The sundown splendid and serene,—Death."

WILLIAM ZENTMAYER.

Correspondence

"PROBLEM IN REFRACTION"

To the Editor:—I should like to make a few comments on "Problem in Refraction," published in the November issue of the ARCHIVES (page 1011). It seems to me that the problem could be more effectively analyzed if the findings were all reduced by transposition to contain the cylinder of the same kind, plus or minus. In this way the range of variation in both the sphere and the cylinder and the tendency of the variations can be more easily seen and understood.

With this method the following results for the right eye are obtained for the six findings, numbered 1 to 6, the correction the patient came with being eliminated. The letter O is used for objective findings and the letter S for subjective findings.

(1)	+ 0.25 sph. ⌒ — 1.00 cyl., axis	10	O
(2)	— 1.50 sph. ⌒ — 0.75 cyl., axis	10	S
(3)	+ 0.37 sph. ⌒ — 0.50 cyl., axis	180	O
(4)	— 0.75 sph. ⌒ — 0.50 cyl., axis	10	S
(5)	+ 0.37 sph. ⌒ — 1.00 cyl., axis	10	O
(6)	— 1.25 sph. ⌒ — 0.75 cyl., axis	180	S

It is seen that the sphere varies between + 0.25 and — 1.50, a variation of 1.75 D., whereas the cylinder varies only between — 0.50 and — 1.00. The questioner's concern, it seems, should be more with the sphere than with the cylinder. With the latter analyzed first, the average of the highest and the lowest in the six findings is — 0.75, which was also the actual finding in two readings. It seems reasonable to consider — 0.75 cyl. as the correct amount. The axis varies between 10 degrees and 180 degrees, and the midway position axis of 5 degrees seems indicated, especially when the axis in the left eye is considered. To return to the sphere, it is seen that the objective findings all were plus, from + 0.25 to +0.37, and the subjective findings all were minus, from — 0.75 to — 1.50. The second (2) finding, — 1.50 sph., might perhaps be eliminated, since the sixth (6) finding, — 1.25 sph., with the same cylinder gave vision of 20/20. There are bound to be some differences between the objective and the subjective findings, but a difference of 1.75, especially in view of the esophoria, needs further investigation, as outlined in the answer.

With the same method of analysis the following results are obtained for the left eye:

(1)	+ 0.50 sph. ⌒ — 0.62 cyl., axis	175	O
(2)	+ 0.12 sph. ⌒ — 0.50 cyl., axis	175	S
(3)	+ 1.37 sph. ⌒ — 0.87 cyl., axis	180	O
(4)	+ 0.50 sph. ⌒ — 0.75 cyl., axis	175	S
(5)	+ 0.62 sph. ⌒ — 0.25 cyl., axis	175	O
(6)	+ 0.50 sph. ⌒ — 0.37 cyl., axis	175	S

Here the sphere varies between + 0.12 and + 1.37, a difference of 1.25 D. The cylinder varies between — 0.25 and — 0.87, and the average finding is about — 0.50 cyl. This may be regarded as the

correct amount of cylinder and should be changed only if, when still more tests are made, there is a definite indication for change.

Here, too, the axis in five out of the six tests is 175 degrees, which can be safely taken as accurate. Making the axis for the right eye 5 degrees gives a condition of symmetric astigmatism, and it is safer to assume symmetry of development unless there are distinct signs to the contrary.

The spherical variation in the left eye of 1.25 D. shows, as in the right eye, that again the objective findings are higher plus values (+ 0.50 to + 1.37) than the subjective findings (+ 0.12 to + 0.50). This corroborates the desirability of more investigations as outlined in the answer.

J. I. PASCAL, M.D., New York.

DR. VERHOEFF'S DISCISSION KNIFE

To the Editor:—I was very much interested in Dr. Verhoeff's letter published in the November ARCHIVES, in which a serrated knife-needle was discussed. Dr. Verhoeff stated: "For over twenty years I have employed a serrated Ziegler knife, which, however, is quite different from . . . the knife depicted by Dr. Parker." Under such conditions one wonders at the statement "Evidently the E. B. Meyrowitz Company failed to inform Dr. Parker of their attempt."

Just why the E. B. Meyrowitz Company should be criticized for failing to inform me of any attempt at making a knife-needle "quite different" from mine is beyond comprehension.

Dr. Verhoeff is to be congratulated on making a knife-needle and using it for over twenty years, which one must assume is the case from the statement "I have attempted to duplicate it, but I have never been able to produce a knife nearly so efficient."

During my past experience of forty years in ophthalmologic practice I have been very well pleased with a knife that will stand up under a half-dozen needlings. Truly a twenty year knife is something to be proud of—that is, if it is used at all. If a knife-needle cannot be duplicated, surely it cannot be sharpened to the original condition; therefore one is left with a feeling of awe at the permanency of its cutting edge. I can easily see why Dr. Verhoeff has not been able to duplicate this knife.

The accompanying illustration of Dr. Verhoeff's knife is enlarged × 11.8. At that, the serrations supposed to be there are so microscopic that one wonders just what and where these serrations are and could be in the tiny blade itself.

Again I congratulate Dr. Verhoeff on making a knife which cannot be duplicated and which has been cutting through the tough Boston capsules for twenty years, as against the commoner knife-needles which are used on our more tender Philadelphia membranes and which, in addition, have to be frequently sharpened.

I must accept Dr. Verhoeff's statements, and until I can prove otherwise I shall have to concede the great superiority of his knife, as I have never used it. Conversely—well, enough is enough.

FRANK C. PARKER, M.D., Norristown, Pa.

News and Notes

EDITED BY W. L. BENEDICT

GENERAL NEWS

National Society for the Prevention of Blindness.—Mason H. Bigelow, of the law firm of Gould and Wilkie, New York, was elected president of the National Society for the Prevention of Blindness by the board of directors at the annual meeting of the society in New York, on Dec. 12, 1940. William Fellowes Morgan, who retired as head of the organization after serving the entire twenty-five years of its history, will have the title of president emeritus.

Mr. Bigelow, a native of Utica, N. Y., was graduated from Amherst College in 1909 and from Columbia University Law School in 1912. He has been a member of the board of directors and executive committee of the National Society for the Prevention of Blindness for the past six years. He is chairman of the executive committee of the Association of the Bar of the City of New York and a member of the executive committee of the New York State Bar Association. He is also a trustee and a member of the executive committee of the New York Public Education Association, a member of the board of visitors of Columbia University Law School and a member of the standing committee of its alumni.

Dr. Edward C. Ellett, of Memphis, Tenn., was elected a vice president to fill the vacancy left by the recent death of Dr. Park Lewis, of Buffalo. Two other vice presidents are Russell Tyson, of Chicago, and Preston S. Millar, of New York.

Dr. Ellett received the Leslie Dana Gold Medal in 1939 for "outstanding achievements in the prevention of blindness and the conservation of vision." He is former chairman of the Section on Ophthalmology of the American Medical Association and a former president of both the American Ophthalmological Society and the American Academy of Ophthalmology and Otolaryngology.

Since its establishment in 1915, the National Society for the Prevention of Blindness has worked in close cooperation with members of the medical profession, especially with ophthalmologists. The society's efforts aim at conservation of vision in a large majority of persons who have normal sight and in a considerable number of partially sighted persons.

The society has approximately 17,500 members and donors throughout the United States. It spent $159,000 during the past year, and a budget of $167,500 was authorized by the board of directors for 1941. Headquarters are maintained at 1790 Broadway, New York. Mrs. Eleanor Brown Merrill is executive director.

Clinical Study in Los Angeles.—The tenth annual midwinter clinical course in ophthalmology and otolaryngology, sponsored by the Research Study Club of Los Angeles, will be held January 20 to 31, inclusive. Guest instructors in ophthalmology will be: Dr. Ralph I. Lloyd, of

Brooklyn; Dr. Walter I. Lillie, of Philadelphia; Dr. Roderick P. O'Connor, of Oakland, Calif.; Dr. Edward Jackson, of Denver, and Dr. Meyer Wiener, of St. Louis. Guest instructors in otolaryngology will be: Dr. Albert C. Furstenberg, of Ann Arbor, Mich.; Dr. Herbert M. Evans, of Berkeley, Calif., and Dr. John F. Barnhill, of Indianapolis.

UNIVERSITY NEWS

Postgraduate Courses at Harvard Medical School.—The Harvard Medical School announces the following postgraduate courses in ophthalmology for the second half of the current school year:

January 6—Fundamentals of Refraction. February 3—Clinicopathological Ophthalmology. February 17—Neuro-ophthalmology and Perimetry. March 10—Ocular Muscles. March 24—External Diseases of the Eye, Ocular Complications in General Disease, and Biomicroscopy, given concurrently. April 21—Ophthalmoscopy and Industrial Ophthalmology, given concurrently. May 19—Principles of Ophthalmic Surgery. June 18—Recent Advances in Ophthalmology. July 7—Visual Optics and Physiology.

CORRECTIONS

In the article by Drs. Bertha L. Isaacs, Frederic T. Jung and Andrew C. Ivy entitled "Clinical Studies of Vitamin A Deficiency: Biophotometer and Adaptometer (Hecht) Studies on Normal Adults and on Persons in Whom an Attempt Was Made to Produce Vitamin A Deficiency," in the October issue (ARCH. OPHTH. **24:** 698, 1940), an error occurred in the units employed in expressing rod and cone thresholds. The label reads "micromillilamberts" but should have been "log micromicrolamberts." The technic used by the authors was the same as that employed by Dr. Selig Hecht and his co-workers, i. e., a three minute light adaptation to 1,500 millilamberts, using for dark adaptation a 3 degree test field 7 degrees out.

In the article by Dr. James W. White, "What Is the Minimum Routine Examination of Muscles?" in the December issue (ARCH. OPHTH. **24:** 1113, 1940), the formula in the last line but one of the fifth paragraph of the section on "Norms" on page 1121 should read:

$$\frac{Pd \times 50}{PcB} + 3 = \text{convergence in degrees of arc}$$

or

$$\frac{\frac{1}{2}\,Pd \times 100}{PcB} + 3 = \text{convergence in degrees of arc}$$

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Blind

SUDDEN BLINDNESS IN CHILDREN. DEDIMOS, Ann. d'ocul. **176:** 605, 1939.

Under this title, which defines only a symptom of the disease without any pathogenic manifestations, there has been described for a long time a pathologic state the dominant symptom of which is the sudden appearance of bilateral blindness. The author reports such an occurrence in a child about 4 years of age.

He concludes that under this syndrome of sudden blindness in children are comprised different pathologic conditions which have a common symptom, namely, the rapid appearance of blindness, which he believes is the result of sudden blocking of the retinal circulation (arterial spasm). The term therefore indicates not a morbid entity but a syndrome consisting of arteritis and a spasm of the central arteries, two pathologic conditions which are frequently present also in adults. The first of these two is due principally to hereditary syphilis and the second to sympathetic vasomotor disturbance, without a syphilitic causation. Other clinical pictures of sudden blindness in children, not accompanied by changes in the retinal vessels and in the fundus, may generally be considered as having a different anatomic basis (retrobulbar neuritis and cortical blindness).

S. H. MCKEE.

Congenital Anomalies

DISLOCATION OF THE LENS, WITH OTHER CONGENITAL DEFECTS: SECONDARY GLAUCOMA. N. B. HARMAN and R. BUXTON, Brit. J. Ophth. **24:** 135 (March) 1940.

A child with dislocation of the lens and other congenital defects had normal parents. At the age of 5 myopia of 18 D. was corrected. There was metatarsus varus of severe degree in both feet. The child's physique was poor and his posture bad. At 11 years of age it was definitely determined that the lenses were dislocated. At a somewhat later period vision in the right eye with a — 25 D. sphere was 6/36, and in the left eye with a — 22 D. sphere, 6/18 (partly).

Still later, as the aphakic gap had increased, he was given a + 11 D. sphere. With this glass vision in the right eye was 6/18, and in the left eye 6/24. At the age of 19 acute glaucoma developed in the right eye. The lens was removed in its capsule, and the prolapse of the vitreous was controlled by a corneoscleral suture. The resulting vision was 6/18.

W. ZENTMAYER.

COLOBOMA OF THE OPTIC DISK. A. BIFFIS, Ann. di ottal. e clin. ocul. **67:** 522 (July) 1939.

A case of typical coloboma of the disk alone is described and illustrated. Areas of chorioretinal atrophy about the disk suggested the possibility that inflammation in utero at the time of development of the disk may have been responsible.

S. R. GIFFORD.

Experimental Pathology

A STUDY OF THE EFFECTS OF LIQUID MUSTARD GAS UPON THE EYES OF RABBITS AND OF CERTAIN METHODS OF TREATMENT. P. C. LIVINGSTON and H. M. WALKER, Brit. J. Ophth. **24:** 67 (Feb.) 1940.

The experimental work reported here was carried out on 23 mature rabbits. The authors describe in detail the technic employed, the results of the clinical examinations, the clinical features of mustard drop contamination and treatment.

The clinical conditions and the histologic changes are illustrated. A special irrigation speculum is also illustrated. The authors provide the following conclusions:

"1. In a small percentage of animals there is some degree of natural resistance which definitely offers a barrier to the effects of liquid mustard.

"2. With rare exceptions, so intense and rapid is the immediate reaction, that no local treatment can be hoped for that will prove helpful at this stage. The interaction of mustard and the secretions of the eye causes an alteration which leaves the mustard inactive as such after fifteen minutes. This alteration is probably an oxidation process which occurs after the initial reaction.

"3. Irrigation with lotions that have a specific destructive effect upon the mustard is not recommended. Sodium bicarbonate 2 per cent seems to be as helpful as any lotion, and there is reason to believe that the dehydrating effect of Bonnefon's solution may have merits. The use of atropine against the irritation of the iris leading to its contraction is clearly of importance.

"4. Antiseptic washes, such as merthiolate 1:10,000, are clearly of value and would certainly be indicated if there was secondary infection.

"5. Oil drops following irrigation appear to exert a favorable effect, and cod liver oil is probably best. There may be value in an oil with a high vitamin A content, but from this investigation we are unable to give any clear ruling on the respective merits of cod liver oil with added vitamin A and cod liver oil of B. P. standard.

"6. There is reason to believe that the spread of corneal ulceration in the human eye could be arrested by the use of the specially designed irrigating speculum just described.

"7. Saturation of the system with ascorbic acid, given intravenously to four rabbits, proved to have a remarkable effect in preventing the

spread of keratitis and the progress of lid inflammation. Although only a few animals were treated in this way, the result in each case so outstrode all others, that it is safe to conclude that this method of treatment is well worthy of trial in any case of mustard contamination of the eye. The characteristic damage observed in the control rabbit of this group and the experience with the other eighteen rabbits of the series lends weight to this argument.

"The result of this investigation, which had to be carried out within a limited period, seems clearly to indicate that there are methods by which the effect of mustard contamination of the eye can be considerably mitigated. So far as we know, there has been no previous attempt to affect the course of mustard injury to the eye through the tissue barrier.

"In the time at our disposal we were unable to investigate the period that could elapse between the injury and the administration of ascorbic acid. This, and the level of effective dosage, must be subjects of further investigation. In the present investigation we used a very high dosage of ascorbic acid.

"It is probable that there are substances other than ascorbic acid, cheaper and more readily available, that might exert a similar effect. This also calls for future study.

"Since the completion of this work some further investigations have been undertaken with the object of discovering whether injections of ascorbic acid up to two hours after mustard injury and at the lower dosage level of 100 mg. is capable of controlling the corneal invasion. Examinations of animals thus exposed and treated proves that this is so.

"At the same time some experiments were done in which sodium thiosulphate (10 per cent) in 500 mg. doses intravenously was given. Examination of these cases indicated that this substance also, given in this fashion, possesses a definite value; but the results obtained from the ascorbic acid treatment are undoubtedly better. No other treatment in the form of lavage or oils was given in either of the latter series of cases."

The article is illustrated.

W. ZENTMAYER.

THE AMINO ACID CONTENT OF THE LENS AFTER ULTRAVIOLET IRRADIATION. A. MILANO, Ann. di ottal. e clin. ocul. **67:** 541 (July) 1939.

The author irradiated one eye of rabbits with an incandescent Osram lamp and with a mercury vapor arc lamp. Exposures at 15 to 20 cm. were continued five to twenty minutes, and usually three to eight doses were given on alternate days. Eleven animals were studied. Complete opacity of the cornea developed in 1 and localized corneal opacities in the others. The lenses of the irradiated eyes showed a slight increase in weight as compared with the control eyes, and a definite decrease in total amino acid. The increase in weight is attributed to increased imbibition of water by the lens proteins and the decrease in amino acids to a photolysis of amino acids with perhaps some escape of these substances through the lens capsule as a result of increased permeability.

S. R. GIFFORD.

General Diseases

OCULAR SCROFULA IN ADULTS. CARLOS CHARLIN, Ann. d'ocul. **176:** 813 (Nov.) 1939.

The basis of the pathogenesis of scrofula rests with the lymphatic tuberculous glands. The complications of the general condition, such as dermatitis, rhinitis, conjunctivitis, and keratitis, are the result of bacillary infection of the glands. Usually the general health is improved by the use of ordinary tonics and cod liver oil, by good elimination and by fresh air, and the special conditions such as conjunctivitis and keratitis, are further helped by local treatment. However, there are cases in which cure is obtained only by specific therapeutic measures, that is, the use of tuberculin, or antigenotherapy.

The details of 4 cases, in which tuberculin was used, are given.

S. H. MCKEE.

Glaucoma

BUPHTHALMOS WITH FACIAL NAEVUS AND ALLIED CONDITIONS. A. J. BALLANTYNE, Brit. J. Ophth. **24:** 65 (Feb.) 1940.

This paper contains the subsequent history of a case previously reported by the author in the *British Journal of Ophthalmology* (**14:** 481, 1931). The patient is now a child 8 years of age. The appearance of the eye which was trephined when the child was 3 weeks old is unchanged. The trephine scar is ectatic and the lens completely opaque. There is perception of light but a doubtful field of projection. Extraction of the lens was attempted through an inferior section, but vitreous was lost, and later in the day an expulsive hemorrhage occurred, requiring enucleation of the eye. Histologic examination revealed a fairly extensive angioma of the choroid. As the facial nevus is congenital, it can be assumed that the choroidal lesion is also congenital. It may be sufficiently developed to establish the glaucomatous process during antenatal life (buphthalmos) while in others the evolution of the neoplasm is delayed until adult life, and then simple or secondary glaucoma results. This, broadly speaking, is the theory advanced by Ginsburg and by Hudelo.

The article contains one illustration.

W. ZENTMAYER.

Lens

INFLUENCE OF DIHYDROTACHYSTEROL ON THE LENS IN TETANY. W. RAUH, Arch. f. Ophth. **140:** 334, 1939.

In 1927 Holtz discovered that irradiated ergosterol cured experimental rickets in rats. Large doses had pronounced toxic effects. The blood calcium rose at the expense of the bones, which were deprived of their calcium. Irradiated ergosterol was thus found to have a pronounced calcium-mobilizing effect, which was subsequently traced to a derivative of ergosterol of the composition dihydrotachysterol. This substance proved to be of great therapeutic value in cases of tetany

(Holtz, 1933), in which it raised the blood calcium, lowered the nervous hyperexcitability and thus prevented convulsions.

The author of the paper under review has studied the effect of dihydrotachysterol on parathyroprival tetany of young rats. He has found that the substance is capable of preventing the outbreak of tetany and the development of opacities of the lens after destruction of the parathyroids by cauterization. "Just as definitely established is in certain stages of tetany cataract the regression of the lens opacities up to the point of perfect clearness of the lens." The protective effect of dihydrotachysterol outlasts by a few weeks the period of its administration. For permanent protection of the lens, the treatment must be kept up continuously.

In tetany of man the protective effect of dihydrotachysterol has been established with certainty. Whether or not tetanic lens opacities in man can be made to disappear by the use of this substance is not known. "That dihydrotachysterol is out of the question as a form of treatment for senile cataract need not be stressed." P. C. KRONFELD.

Lids

ROENTGEN THERAPY FOR FURUNCLES AND STYES. L. HAMBRESIN, Ann. d'ocul. **176:** 803 (Nov.) 1939.

In the large majority of cases infection of the sebaceous glands of the lids recedes rapidly after treatment with moist, hot applications of slightly antiseptic fluid, which is sometimes assisted by a small incision or puncture with a fine galvanocautery. It is recognized, however, there are cases also in which cure is difficult and takes place only after lengthy treatment. These conditions may also, in exceptional instances, be complicated by abscess of the orbit, phlebitis of the ophthalmic veins and thrombosis of the lateral sinus.

It is for this reason that the author brings forward a treatment which has been little used and with which his results have been satisfactory. He first gives a historical retrospect, then the technic of the treatment, the indications, contraindications, results and advantages. He believes that roentgen rays have given excellent results and suggests that perhaps they would be equally beneficial in cases of acute dacryocystitis, orbital periostosis and cellulitis of the orbit, at least in the early stages.

A bibliography accompanies the article. S. H. MCKEE.

Neurology

POSTHERPETIC NEURALGIA IN THE DISTRIBUTION OF THE CRANIAL NERVES. O. R. HYNDMAN, Arch. Neurol. & Psychiat. **42:** 224 (Aug.) 1939.

Deep pain behind the eye is a common symptom of postherpetic neuralgia. It was not relieved by cutting the sensory root of the trigeminal nerve, but was relieved by anesthesia of the supraorbital

region with procaine hydrochloride and by section of the ophthalmic and maxillary nerves just distal to the gasserian ganglion.

The author concludes that the pain and hyperesthesia of postherpetic neuralgia are mediated by afferent sympathetic nerves which are carried to the gasserian ganglion by the ophthalmic and maxillary nerves, but do not necessarily leave the gasserian ganglion by the sensory root, and that the most certain way of elimination of the pain carried by the sympathetic nerves was by removal of the stellate and several upper thoracic sympathetic ganglions on the ipsilateral side. R. IRVINE.

PRESENT STATUS OF KNOWLEDGE ON THE ANATOMY AND FUNCTIONS OF THE EXTERNAL GENICULATE BODY IN MAN. MANUEL BALADO, Arch de oftal. de Buenos Aires **14:** 205 (March) 1939.

Of late a series of investigations have been published on the function of the external geniculate body, with reference to its segmentation and its afferent and efferent connections. These investigations point to the correspondence of the different segments, those of the retina on one hand and of the area striata on the other. That some layers of the external geniculate body are connected with the contralateral retina and some with the homolateral retina has been confirmed in several species of monkey and in man. The literature on the subject is reviewed in detail.

Reference is likewise made to the relations of different portions of the external geniculate body to different portions of the calcarine fissure.

The anatomic and clinical data in relation to the cortical localization of the macula are few and are abstracted by the author; they point toward the projection of the macula along all of the calcarine fissure, instead of only at the apex of the occipital lobe, as hitherto held.

Apart from the aforementioned segmentation, the upholders of a bilateral representation of the macula maintain that part of the geniculate body sends fibers also to the occipital lobe of the opposite side through the corpus callosum; the author, however, is inclined to explain the clinical symptoms by the extension of macular vision all along the calcarine fissure, the nonexistence of the fasciculus cruciatus being, moreover, proved by the experiments of Maison, Settlage and Grether, in which after extirpation of an occipital lobe and the opposite optic tract vision was reduced to simple perception of light and dark, thus explaining the preservation of macular vision in cases of cortical hemianopia.

This is all the more evident in relation to the external geniculate body, different strata having been pointed out relative to the approximate reproduction in it of different regions of the visual field. The author refers to his own studies in this connection, based on degenerations in pathologic cases and on the anatomicoclinical study of a case in which hemianopic scotoma was produced by arteritis of the middle artery with destruction of the internal portion of the external geniculate body. The lack of proof in some of the reported cases is attributed to the fact that graduated perimetry was not used in the study of the defects of the visual field. The author next describes in detail the different forms of cells and fibers and their grouping into layers and discusses the pathologic lesions resulting from deep lesions of vascular origin and the more superficial

ones due to meningeal involvement. These explain the rarity of absolute macular scotomas in cortical lesions and their frequency in those of the optic tracts.

The author finally discusses the connections of the giant cells of the external geniculate body. Some authors hold that the fibers proceeding from them pass to the cortical striate region and others that they pass to the corpora quadrigemina. The author favors the first view.

The paper is illustrated with numerous case reports and cuts of pathologic lesions and has an extensive bibliography. C. E. FINLAY.

Ocular Muscles

FREQUENCY OF BLINKING AS A CLINICAL CRITERION OF EASE OF SEEING. M. LUCKIESH and F. K. Moss, Am. J. Ophth. **22:** 616 (June) 1939.

Luckiesh and Moss agree with previous workers that blinking is closely related to mental tension and is a kind of relief mechanism. They also agree that an increase in blinking is in part due to factors associated with fatigue. They base these conclusions on tests occurring during five minute periods at the beginning of and at the end of an hour's reading under different illuminations and following the use of plus and minus lenses. W. S. REESE.

CONVERGENCE DEFICIENCY: THE CONDITION, ITS OCCURRENCE IN PRIVATE PRACTICE, AND THE RESULTS OF TREATMENT. IDA MANN, Brit. M. J. **1:** 208 (Feb. 10) 1940.

According to Mann, patients with convergence deficiency show a divergence of 6 degrees (exophoria) at reading distance and an absence of power of voluntary convergence and occur in her private practice in the percentage between 2 and 3. The cases are analyzed according to age, refraction and type of patient.

The cerebral localization of the centers concerned in convergence and the evolutionary value and meaning of the movement are considered. Treatment and its results are dealt with. The conclusions agree in the main with those of other observers, in that it can be shown that the condition is due to a developmental lag (functional, not anatomic) and that neither age nor accompanying error of refraction has any influence on its occurrence. In most persons educative treatment of the cerebral centers and facilitation of the reflex by exercises have a marked beneficial effect. ARNOLD KNAPP.

Operations

RESECTION OF ANTERIOR STAPHYLOMA OF THE CORNEA BY MEANS OF GRADUAL INCISIONS. N. I. SHIMKIN, Brit. J. Ophth. **23:** 671 (Oct.) 1939.

Shimkin seeks to avoid the loss of vitreous which is likely to follow the usual method of removing the corneal staphyloma by one incision.

The essential of the author's method is that the staphyloma of whatever size is resected by gradual short incisions of 1.5 to 2 mm. wide instead of all at once. The margins of each incision are immediately drawn together by sutures. The operation is described in detail, and the various steps are illustrated.

W. ZENTMAYER.

Physiology

THE MECHANISM OF DARK ADAPTATION: A CRITICAL RÉSUMÉ. R. J. LYTHGOE, Brit. J. Ophth. **24:** 21 (Jan.) 1939.

This review deals with the physiologic theories of dark adaptation and is not concerned with the technics of measurement or the vast amount of literature on subjective measurements. The importance of a thorough knowledge of the basic physiology is stressed because of the frequent "black-outs" in European cities. The duplicity theory is briefly outlined and then subjected to a critical analysis. The author aptly points out that vision cannot be simply described as "photopic" and "scotopic" —that there is considerable overlapping in the function of the rods and cones. The lack of correlation between the concentration of visual purple and the light threshold during the course of dark adaptation offers another difficulty in accepting dark adaptation as a purely photochemical bleaching and regeneration of visual purple.

The author reviews the generally accepted theories of the kinetics of the visual purple and shows that the underlying chemical change in dark adaptation is not necessarily unimolecular or bimolecular. This section on visual purple is the best résumé to appear in the literature within the past few years.

The author introduces some new concepts in discussing the possible nervous changes during dark adaptation. His theories are based on the subjective experiments on flicker, intensity discrimination, binocular matching and the objective experiments of Granit and others on the electroretinogram of the frog. Nervous interaction or convergence in the retina was first demonstrated by Adrian, and Lythgoe has an illustration in the text to demonstrate his own suggestion that during dark adaptation there is an increased convergence of the retinal fibers. The theory is novel, but the proof will lie in subsequent objective experiments.

To those who are interested in the basic physiology of vision, this review is to be highly recommended. Articles of this type appear all too infrequently in the ophthalmic literature.

R. MCDONALD.

Refraction and Accommodation

SPHERO-CYLINDRICAL CONTACT LENSES: A PRELIMINARY NOTE. F. A. WILLIAMSON-NOBLE, J. DALLOS and I. MANN, Brit. J. Ophth. **24:** 43 (Jan.) 1940.

It has been noted that in some cases in which a contact glass is applied vision can be further improved by the addition of a cylindric lens in a trial frame.

Such astigmatism may be due to (1) aberrations in the curvature of the posterior surface of the cornea, (2) aberrations in the curvature

of the anterior and/or posterior surface of the lens, (3) radial errors due to the center of the lens not coinciding with the optical axis of the eye, (4) variations in the refractive index of the lens in different meridians and (5) tilting of the lens.

None of these can be corrected by a contact lens with spherical corneal surfaces. It has proved possible to grind such a correction on the posterior (concave) surface of the lens; but here an interesting complication arises, because one is dealing with the difference between the index of refraction of glass and of the saline solution which fills the space between the anterior surface of the cornea and the posterior surface of the contact lens.

Calculation has shown that the increase in strength is approximately 2.5, i. e., a cylinder of 2.5 D. ground on the posterior surface of a contact lens will produce the effect of a 1.0 D. cylinder on the anterior surface.

Several cases are reported in which improvement in vision resulted by the addition of a cylinder.

W. ZENTMAYER.

TRANSITORY MYOPIA: REPORT OF THREE CASES. R. MATTSSON, Acta ophth. **17:** 314, 1939.

The author reports 3 cases in which myopia of from 2.5 to 5 D. promptly developed in adults after taking small doses of sulfanilamide preparations. In each instance the myopia disappeared after a few days. Careful studies of the refraction seemed to eliminate the possibility that a spasm of accommodation was responsible for the myopia in any of these cases. Chemical analyses of the blood of 1 patient showed no abnormality of the sodium chloride or of the plasma protein content. As these patients had on other and previous occasions taken some form of sulfanilamide, the author believes it possible that the reaction may have been allergic in nature, taking place in the lens.

O. P. PERKINS.

Retina and Optic Nerve

PSEUDOTUMOROUS DEGENERATION OF THE MACULA (DISCIFORM). A. MAGITOT, Ann. d'ocul. **176:** 721 (Oct.) 1939.

This curious disease, the first anatomic descriptions of which were published in 1919 and 1923, was described previous to this clinically under a number of different terms. Central chorioretinitis with arteriovenous lesions is the name used by Oller, while Michel called it fibrochondroma. Axenfeld called it exudative retinitis with osseous formation. A summary of previous cases reported is given, and a case is reported in detail.

Magitot says the clinical and anatomic study of the globe with pseudotumorous degeneration of the macula led him to the belief that the mass consisting of an accumulation of pigmented epithelial cells, of degenerated nerve cells of the retina and of microglia cells, all mingled together in a tissue taking on the reactions of the conjunctiva, must mean a manifestation of pathologic involvement of the pigmented epithelium. The mesodermal lamina of the membrane of Bruch forms a continuous partition between the pseudotumor and the choroid.

Magitot explains the pathogenesis as follows: Under the disturbance in the nutritive channels by the functional absence of the corresponding choriocapillaris, the cells of the pigmented epithelium become the site of diverse modifications. There is a change in the form of the nucleus, the pigment becomes rarefied and there is production of hyaline verrucosities, with secretion of an abundant and thick fluid. At a later stage the cells of the epithelium proliferate, become mobile, penetrate into the degenerated retina and undergo hyaline degeneration. Some have lost their pigment; others have conserved a few grains.

The pseudoconjunctival tissue which has collected the cells of the tumor is not mesodermal tissue, and the tissue which takes the red stain of Van Gieson and the blue of the Mallory stain has but the appearance of conjunctival tissue. It is formed by epithelial cells, and after passing through the semiliquid stage it takes on a fibrous aspect.

Without wishing to generalize, it seems, however, following the descriptions of other published anatomic studies, that this pathogenesis of pseudotumorous degeneration may be applied to the majority of cases. The participation of the choroid in the formation of the tumor is far from certain.

The degenerative lesions called circinate differ from those of pseudotumorous degeneration, and while the two conditions arise from the same cause, the mechanism of their formation is different. They may exist together, but it is more probable that the first type develops into the second.

A bibliography and four plates accompany the article.

S. H. McKee.

Retinal Arteritis Causing Bilateral, Symmetric Horizontal Hemianopia. P. Mastier and G. Farnanier, Bull. Soc. d'opht. de Paris **51**: 197 (March) 1939.

A patient while working noted sudden loss of both lower fields of vision. He consulted a general practitioner, who found an arterial tension of 270 mm. Treatment gave relief, but three months later a similar attack occurred. There was no headache or motor or sensory loss, and the man continued at work. He was 70 years of age and appeared robust. His blood pressure was 230 systolic and 100 diastolic. The urine and blood chemistry were normal. The visual acuity was 20/20 for each eye. The ophthalmoscope revealed normal maculas, but above the macula, especially in the temporal region, were numerous hemorrhages and exudates with spasm of the superior temporal arterial branches. Arteriovenous nicking was much in evidence. The arterial retinal pressure was 90 mm. Treatment with acetylcholine and papaverine was without avail. Charts of the visual fields and photographs of the fundi are included.

L. L. Mayer.

Evolution and Prognosis of Choked Disk. R. Laje Wsekamp, Arch. de oftal. de Buenos Aires **14**: 303 (April) 1939.

After a general consideration of the development, causes and symptoms of choked disk, the author deals with the problems arising from

choked disk associated with various conditions. He studied these factors separately in cases of suppurative encephalic lesions, sinus thrombosis, tumor of the brain with evolution of the corresponding functional disturbances, syphilis and tuberculosis of the central nervous system and cerebral hemorrhage. He considers the therapeutic indications in the different varieties of choked disk.

C. E. FINLAY.

ADHESION OF THE VITREOUS TO THE EDGE OF A RETINAL TEAR IN RETINAL DETACHMENT. J. BOECK, Arch. f. Ophth. **140:** 468, 1939.

In 2 cases of retinal detachment examination of the fundus with the slit lamp and the angulated corneal microscope of Lindner revealed adhesions (pictured) between the vitreous and the peripheral edge of a retinal tear. After operative procedures resulting in complete reattachment of the retina, these adhesions were still present.

P. C. KRONFELD.

Trachoma

CULTURE IN VITRO OF THE CORPUSCLES OF TRACHOMA. L. POLEFF, Brit. J. Ophth. **23:** 738 (Nov.) 1939.

Poleff presented at the meeting of the International Organization Against Trachoma a series of photomicrographs exhibiting typical pictures of various stages of the evolution of trachoma corpuscles in vitro. According to their cycle of evolution observed in vitro, these parasitic atoms probably belong to the class of ultraviruses, but their exact biomorphologic classification, virus or Rickettsias, seems to be uncertain.

The author is of the opinion that the rickettsia-like corpuscles described by Busacca, and later by Cuénod, at any rate those which are not debris, cellular or otherwise, are identical with the inclusion bodies of Halberstädter and Prowazek at certain stages of their evolution.

The article is illustrated.

W. ZENTMAYER.

Tumors

THE X-RAY TREATMENT OF MALIGNANT TUMORS IN THE REGION OF THE EYES. D. W. SMITHERS, Brit. J. Ophth. **24:** 105 (March) 1940.

Smithers states that the effect of radium and of roentgen rays on the eye is essentially the same and that there is an absolute relation between the dose of radiation given and the pathologic changes produced.

The immediate danger to the eye is severe conjunctivitis followed by corneal ulceration; the late danger is the development of cataract.

The author gives the following summary of his paper:

"The effect of X-rays on the eyes and the radiation methods of treatment of malignant growths in their vicinity are discussed briefly. Previous methods of eye protection are referred to, and new lead-covered contact 'perspex' shells for protection of the eyes in short distance, low-voltage X-ray treatment are described. The advantages of this form of X-ray therapy and the results obtained in the treatment of

tumours of the lids and canthi during the last four years at the Royal Cancer Hospital (Free) are discussed."

The text contains numerous illustrations. W. ZENTMAYER.

REABSORPTION GRANULOMAS OF THE LID AND CONJUNCTIVA. GEORGIADES, Ann. d'ocul. **176:** 675 (Sept.) 1939.

The granulomas of reabsorption, like those of foreign bodies, are commonly seen and well recognized in general pathologic study. For many years pathologists have been struck by the presence of giant cells about foreign bodies accidentally introduced into tissue. These are most characteristic of granulomas and play an active part in the absorption of foreign bodies.

These granulomas are seen frequently in the ocular field and are more important here than in other parts of the body. They have not as yet been the subject of a systematic study.

In the first part of the paper absorption granuloma in general is taken up, its nature, histogenesis, evolution and different aspects being dealt with. The absorption granulomas brought on by exogenous foreign bodies are then discussed. Next granulomatous absorption about the tissues, modified by a process of necrosis, is considered.

The author concludes that absorption granulomas of the lids and conjunctiva are the most frequently seen among those of the eye. Their study is important, as the diagnosis often is difficult. They have been confused with syphilitic lesions, tuberculosis, trachoma and true neoplasms. In the presence of nodules of different sizes, especially about the lids and conjunctiva, it is necessary to think of the possibility of absorption granuloma provoked by an exogenous foreign body or by an endogenous inert substance difficult to absorb. Exogenous foreign bodies provoking such absorption granulomas consist of metallic splinters, small pieces of wood, eyelashes, catgut or silk threads and other articles. For diagnosis, a histologic examination is necessary.

S. H. MCKEE.

Sympathetic Ophthalmia

HISTOLOGIC AND CLINICAL RESEARCH IN SYMPATHETIC OPHTHALMIA. S. GÖRDÜREN and H. SOHR, Klin. Monatsbl. f. Augenh. **102:** 830 (June) 1939.

The authors examined histologically 428 eyeballs with perforating traumatic or operative wounds for symptoms of sympathetic inflammation. Of this number, 323 eyes were removed at the ophthalmic clinic of the University of Berlin. Positive symptoms were found in 0.25 per cent of the eyes with penetrating injuries and in 0.045 per cent of the eyes that were operated on. Clinical symptoms were observed during treatment in one half (or 0.12 per cent) of the injured eyes and in all of the eyes operated on. Examination of 60 per cent of the patients with positive symptoms or of those whose eyes were removed for suspected sympathetic ophthalmia showed no involvement of the second eye after two years. Three tables illustrate the findings. No conclusion was arrived at with reference to the time which may safely elapse before enucleation.

K. L. STOLL.

Society Transactions

EDITED BY W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

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Oct. 17, 1940

Pneumococcic Infection of the Conjunctiva Followed by a Pneumococcic Meningitis. DR. CARROLL R. MULLEN and DR. JOSEPH R. WEINTROB.

In reviewing the case of a child who died from meningitis of pneumococcic origin, it is of more than striking ophthalmologic interest to note that the first complaint and sign appeared in pneumococcic conjunctivitis of one eye. While this local condition cleared rapidly and quite satisfactorily under treatment, the signs pointing to meningitis appeared while the child was still in the hospital. It is difficult to state definitely that the conjunctivitis was the origin, or source, of the infection which resulted in meningitis. However, it is important to note that this child was in apparent good health until the onset of the conjunctivitis, which was followed in a few days by the fatal attack of meningitis.

This is a case report from the ophthalmologic service of Dr. Carroll R. Mullen and the pediatric service of Dr. Ernest L. Noone at the Philadelphia General Hospital.

The patient was a 1 month old boy. On Sept. 19, 1940, a redness developed in the right eye, which was treated at home with boric acid. The following morning the patient was admitted to the Philadelphia General Hospital with a markedly inflamed and swollen right eye. The lids were thickened and angry red. The conjunctival sac was bathed with pus. A smear showed many gram-positive diplococci, resembling pneumococci. Otherwise the child was entirely well, with no evidence whatsoever of meningitis or any other disorder. The patient was treated with sulfathiazole (2-sulfanilamidothiazole), administered by mouth, and by irrigation with physiologic solution of sodium chloride followed by sulfathiazole solution, as well as with 0.25 per cent atropine sulfate, three times a day and the frequent application of cold compresses.

In forty-eight hours the eye was entirely normal, and all treatment was stopped except irrigation every three hours. The child appeared entirely normal. In the following twenty-four hours, his temperature rose to 103 F., and he began to have frequent convulsions.

A tentative diagnosis of meningitis was made, and was borne out by an examination of the spinal fluid, which revealed large numbers of pneumococci, type V, as well as many pus cells.

Despite three blood transfusions and large doses of pneumococcus serum type V and the administration of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) by mouth in adequate doses, the child's condition became progressively worse, and death ensued.

Postmortem examination confirmed the diagnosis, having shown a plastic purulent meningeal exudate, which contained on culture Pneumococcus type V. Autopsy did not reveal a course or mode of extension from the eye, if such was the focal point.

DISCUSSION

DR. ERNEST L. NOONE: The question of primary importance is whether the conjunctivitis was the source of the infection causing the meningitis or whether a hidden infection of the postnasal space, possibly with invasion of the infantile ethmoid cells, initiated the conjunctivitis and meningitis. I cannot answer that question. When I saw the patient, the physicians in the department of ophthalmology had cleared up the conjunctivitis, and the eye was in excellent condition. There were mucus and pus in the postnasal space, but that might have come from a later secondary infection.

Dr. Mullen and I were told in the autopsy report that the area in the region of the sphenoid sinus was red and spongy, but that is the usual appearance of that area in babies as young as the one in this case. The formation of a thrombus found in the longitudinal sinus was evidently a terminal event, secondary to circulatory failure.

The organism recovered was the type V pneumococcus. Type V pneumococcus is found more frequently in children over 2 years than in babies of the age of this one. In the treatment of the child rabbit serum type V and sulfapyridine were used. Previously sulfathiazole had been employed. Sulfathiazole may well have had a deterring effect on any postnasal infection or even on an oncoming meningitis. It is supposed that sulfathiazole is not very effective in the treatment of meningitis, because of the low concentrations in the spinal fluid, but I do not believe that any one has as yet shown the concentration of sulfathiazole that is effective.

I am not at all convinced of the wisdom of the cisternal punctures performed on the baby on the last day. In a baby 5 weeks of age the cisterna is a very small space and puncture is fraught with danger. If one desires puncture in such a case, ventricular puncture might be more in order. Some years ago physicians were a little more inclined to do cisternal punctures. Now, with a specific serum and with chemotherapy, one endeavors to build up an adequate concentration of the therapeutic agent in the spinal fluid and is less inclined to resort to drastic measures. Of course, I do not think for a moment that the cisternal drainage had anything to do with the final outcome of this case.

DR. CARROLL R. MULLEN: The usual source of meningeal infection is the middle ear. In this case the nasopharynx was explored and no involvement could be found. I have never known a case in which a primary conjunctival infection has resulted in an attack of meningitis.

Dr. Weintrob and I are not insisting that this conjunctival infection was the source of infection. Sulfathiazole was used immediately on admission, locally and by mouth. I have been using sulfathiazole with much success in the treatment of some conjunctival infections; it is used both internally and externally in solution. We did not at all suspect the presence of meningitis. The child came to us by way of the pediatric outpatient unit, where a careful examination was made and all unusual signs were looked for.

DR. WARREN S. REESE: Were bacteriologic studies made of the nasal and throat secretions?

DR. MULLEN: No, there were none made.

DR. BRAV: I should like to ask, how did you account for the high temperature of the patient when you considered the condition to be localized?

DR. WEINTRAUB: The rectal temperature was above the normal of 99.6 F. only about 0.6 to 0.7 of a degree. It therefore aroused no unusual suspicion on our part.

Microphthalmos with Tumorlike Neuroglial Proliferation. DR. W. E. FRY.

The present report concerns a case of microphthalmos with marked intraocular changes. That the changes were not associated with the presence of a cyst was shown by clinical and histologic examination.

The eye to be described was enucleated by Dr. J. S. Shipman at the Wills Hospital, and the present report is made with his permission.

The measurements of the eye were well below those of a normal eye at birth. The anterior-posterior diameter was 8 mm. and the lateral 8.5 mm. Corresponding minimal dimensions of a normal eye at birth would be 12.5 mm. anterior-posterior and 14.5 mm. lateral. The cornea was 7.5 mm.; the cornea of a normal eye at birth measures 10 mm.

Without describing the eye in detail, the following observations should be pointed out: The choroid appeared to be normally formed and the corneal stroma and the sclera well developed. There was no lens and no lamina cribrosa. The hyaloid artery was present. The angle of the anterior chamber was poorly developed and appeared similar to illustrations of the angle of a 5 month fetus. Normal iris tissue was not present, but a band of tissue separated the aqueous from the vitreous chamber. This band consisted of collagenous tissue on the posterior aspect. The pigmentary epithelial layer of the retina was present. The whole of the vitreous cavity contained a mass of tissue, which was partly collagenous tissue surrounding the hyaloid artery and partly proliferated neuroglial tissue. Groups of cells similar to those which make up the internal nuclear layer were present. There was no separation into internal and external nuclear layers. There were no rosettes.

The marked change in the posterior part of the eye appears to represent defective development of the inner layer of the secondary optic vesicle, with a secondary proliferation of neuroglial tissue. Vilhagen reported a somewhat similar case but in his case there was less extensive

neuroglial proliferation. The lack of a lens represents defective development of the surface ectoderm. The frequency with which cataract is associated with microphthalmos indicates that defective development of the associated ectoderm must be common.

DISCUSSION

DR. J. S. SHIPMAN: The child presented typical microphthalmos, and the eye was somewhat irritable. I removed it for cosmetic reasons and inserted a gold ball into Tenon's capsule. The pathologic conditions as demonstrated were totally unknown to me and were not suspected.

DR. PERCE DE LONG: Anomalies such as that described result from faulty development of the primary optic vesicle. One type is spoken of as anophthalmos; in this condition the primary optic vesicle has not developed. Misdirected or faulty development of the primary optic vesicle sometimes leads to cyclopia and sometimes to diprosopia, or two-facedness. This type is known as micropthalmos. In anophthalmos neurologic elements are absent. This feature distinguishes that condition from microphthalmos. By microphthalmos is meant smallness of the eye or maldevelopment of an eye which contains neurologic elements. The microphthalmos observed in some maldeveloped eyes, in which the ectodermal layer has not been pushed back, is spoken of as a cystic type. In a second type the ectodermal layers are involuted and become adjacent to the pigmentary layer of the choroid or the retina. I think this is the type to which the anomaly in this case belongs, for here, you will notice, there was a sort of false retinal detachment. The so-called glial tissue was the result of some insult. In this type of deformity there are usually associated colobomas of the iris, lens and choroid (as Dr. Fry has said), but none were present in this specimen.

DR. FRANCIS HEED ADLER: I should like to ask how often the condition occurs. Was this a retinoblastoma or some other form of tumor?

DR. W. E. FRY: I don't believe that this represents any real tumor formation. Neuroglial hypertrophy in nerve tissue corresponds to fibrous tissue hypertrophy elsewhere. You might consider a keloid a tumor or a fibroma a tumor. I certainly do not believe that this was a malignant growth. I don't believe it represents a neuroblastoma; the neuroepithelial characteristics were absent.

Surgical Treatment of Neurofibromatosis (Plexiform Neurofibromas).
DR. EDMUND B. SPAETH.

Plexiform neurofibromatosis, a subdivision of those conditions grouped with von Recklinghausen's disease and neuroma, is surgically a condition characterized by the formation of a neurofibroma of the terminal fan of the superficial nerve. Eleven such cases are presented in this paper to illustrate the various defects which need correction and the necessary surgical procedures.

DISCUSSION

DR. ISAAC TASSMAN: I should like to know over how long a period Dr. Spaeth collected his unusually large number of cases of neurofibromatosis. As 1 patient did show a pigmentation about the region of the knee joints, I should like to know whether it was possible to determine in the cases of any others if tumor formations were present in any other part of the body. I should also like to ask whether the eyegrounds were examined and whether a report of the findings in the good eyes was made.

DR. EDMUND B. SPAETH: All these were cases of plexiform neurofibroma and no other tumor formations were present. Perhaps 50 per cent of the patients showed café au lait spots. In all the instances the opposite eye was normal. The collection of these cases extended over a period of twenty years.

Book Reviews

Ueber die Entwicklung und den heutigen Stand der Hornhauttransplantation. (Supplement 7 of Klinische Monatsblätter für Augenheilkunde, 1940). By Zdravko Nizetic. Price 3.60 marks. Pp. 73, with 34 illustrations and 5 tables. Stuttgart, Ferdinand Enke, 1940.

This is a monograph dealing with the subject of corneal transplantation. It is divided into eleven chapters.

In the first chapter a brief review of the literature is made.

In the second chapter the different types of corneal transplantation are discussed. The author believes that in autokeratoplasties success ought to be obtained in 95 per cent of cases and that in homokeratoplasties success may be expected in 80 per cent. Of the types of autokeratoplasty, Kraupa's technic by rotation is the one that gives best results. Of the homokeratoplasties, the partial penetrating type is the simplest and the one that gives best results.

In the third chapter donor's material, technic of transplantation and size and fixation of the graft are considered. The author believes cadavers to be the best source for obtaining corneal grafts. Credit is given to Filatov for advocating and popularizing the use of cadaver corneas. Nizetic does not believe that the cornea preserved in solution of formaldehyde is suitable for corneal transplantation. In 2 cases in which corneas preserved in solution of formaldehyde were used the transplants became detached. A study is made of cultures and scrapings taken from cadavers, those with too many leukocytes and bacteria being eliminated. The author obtains several grafts from the same eye. The grafts are preserved in a Petri dish at a temperature of 4 C. Experiments carried out to determine the vitality of the grafts proved that the cornea preserved metabolic activity for about ten days. In regard to technic, Nizetic prefers the use of a hand trephine of his own design to that of von Hippel. He prefers to fasten the graft in position by means of a conjunctival flap instead of by sutures. The sutures of Elschnig and Castroviejo are described. Nizetic does not seem to have had any experience with the technic of Castroviejo, but quotes Arruga and Green as saying that his technic is better than that of Castroviejo. As to the size of the graft, the author uses a graft varying between 3 and 5 mm. in diameter. The graft ought to be in contact with healthy cornea in order to obtain the best results. He does not believe in the necessity of making the graft of a different size than that of the defect in the cornea of the host. He claims to have obtained good results with use of a graft of the same size. When a graft smaller or larger than the defect in the cornea of the host was used he had more complications.

In the fourth chapter the operations of Elschnig and Filatov are described. Nizetic's operation, which is a modification of that of Filatov, is also described. Instead of using the prophylactic spatula of Filatov, Nizetic employs a knife of his own design, which is used to make a puncture and counterpuncture in the cornea and is left in place to protect the intraocular structures while the leukoma is dissected with the hand trephine, also of his own design. The graft is held in position by a conjunctival flap, similar to the one used by Filatov. With respect to

complications during the operative procedure, the author mentions prolapse of the iris and claims that the use of his knife prevents this complication. Injuries of the lens and iris, a graft of different size than that of the defect and prolapse of the vitreous, which complications he claims can be avoided by the use of his knife, are also mentioned.

The author examines the eye twenty-four hours after the operation to see if the graft is in good position. If not, it should be replaced in the opening in the cornea of the host. Early and late postoperative complications, such as the formation of opaque membranes behind the graft and early and late opacification of the graft, are discussed in detail. The author quotes Elschnig, who stated that from nine to twelve months are necessary before the permanent results of a corneal transplantation is known. The different means used to clear up grafts that have become more or less opaque are discussed in detail, but the author does not feel that any method is very successful for improving a graft that has a tendency to remain cloudy.

In the fifth chapter the histologic changes in a case studied by Filatov are mentioned. The author has not been able to study microscopically any cases of his own.

In the sixth chapter infra-red photography is discussed. According to the author, infra-red photography is particularly useful in cases of dense leukomas, to find out the state of the iris and lens.

In the seventh chapter, indications for keratoplasty for visual, tectonic and curative purposes are discussed in detail.

In the eighth chapter statistics from the author's experience are given. He has performed operation in 90 cases, in 15 of which (16.6 per cent) a clear graft was obtained; in 32 cases (35.5 per cent) the grafts remained translucent; in 40 cases (44.4 per cent) the grafts became opaque; in 3 the grafts were lost, and in 2 they became infected.

In the ninth chapter preliminary operations and treatments required to improve unfavorable eyes and prepare them for final keratoplasty for visual purposes are discussed in detail. The author has not had any success with these preliminary procedures.

In the tenth chapter the author emphasizes the great social importance that keratoplasty has, quoting Filatov, who claimed that in from 45 to 50 per cent of all cases of blindness the cause is a corneal condition.

In the eleventh chapter the author summarizes his articles briefly. Contrary to what has been said by some ophthalmic surgeons that keratoplasty is in the experimental stage and gives poor results, the author states that when keratoplasty is performed on favorable eyes success may be expected in a high percentage of cases.

The monograph ends with a complete bibliography of all the articles published on the subject of corneal transplantation from 1920 to 1939. However, of the hundreds of papers included in the bibliography, apparently few have been consulted in writing the article. Throughout the monograph only about a dozen authors have been mentioned. The monograph contains apparently only the experience of the author, which is limited to the technic of Filatov and his modification. The criticisms of other operations that he makes seem to be based not on personal experience but on the confidential reports given to him by persons who, judging by what has been published, do not seem to be qualified to give expert advice in regard to corneal transplantation.

R. CASTROVIEJO.

Pathologisch-anatomische Untersuchungen über die Beziehungen der Gefässsklerose des Auges zu arteriosklerotischen Veränderungen im Gehirn, im Herzen, in den Nieren, und an den grossen Körperarterien. By Dr. F. Rinteln. Price 5.60 Swiss francs. Pp. 48. Basel: S. Karger, 1939.

The question, summarily indicated in the title of this brochure, is an important one, as the clinician is practically interested in knowing whether ophthalmoscopic finding of arteriosclerotic changes in the fundus oculi justifies one in assuming the presence of similar vascular anomalies in the brain.

It has been generally assumed that an analogy of this nature does exist, although, as the author states, it has never been subjected to a systematic study and test on the basis of pathologic histology, macroscopic and microscopic.

Rinteln has broadened the scope of the investigation to include the kidney, the heart and the larger systemic vessels. His material, from 45 postmortem examinations, includes cases of "simple" senility, generalized arteriosclerosis without hyperpiesis, contracted kidney with high blood pressure and arteriosclerosis with a similar anomaly and some cases in which there was no vascular pathology (*Gefässnormalen*). The most important conclusion to be drawn from this investigation is that one is not justified in assuming from the presence of arteriosclerotic changes in the retinal arteries a similar condition in the blood vessels of the brain. This applies to the large basal branches as well as to the smaller vessels of approximately the same caliber as that of the lesser ramifications of the retinal vascular tree. Conversely, one may find marked sclerosis of both categories of cerebral blood vessels without any evidence of retinal arteriosclerosis. In retinal arteriolar sclerosis one is dealing not with true hyalinization but with an increase of the collagenous connective tissue between the intima and the delicate elastica interna. Retinal arteriosclerosis is generally associated with a similar process in the choroid, but even when this was marked no sclerosis was observed in the vessels of the iris and ciliary body. Sclerosis of the central artery of the retina itself was not present in a single case. Severe retinal arteriosclerosis with fatty degeneration of the hyperplastic intima and occlusion of the lumen was found, almost without exception, only in cases with associated hypertensive retinopathy. This sclerosis may involve even the finest peripheral twigs of the retinal arteries. In all cases of severe diabetes there was cystoid degeneration and proliferation of the pigment epithelium of the iris, but these changes were never noted in cases of nondiabetic conditions. Last, but not least, in the presence of severe sclerotic changes in the retinal arteries one is entitled to assume, with a high degree of probability, the presence of renal arteriosclerosis. "The retina is not a mirror of the brain, but it definitely is a mirror of the kidney!"

PERCY FRIDENBERG.

Valorización de las incapacidades en los accidentes oculares del trabajo. By A. Tiscornia, E. Bertotto and J. V. Artiz. Pp. 154. Buenos Aires, 1939.

This paper is a contribution to projected reforms in the laws governing workmen's compensation for injuries to the eyes in Argentina. The

authors advocate changes in several articles of the present rules for compensation and advise the inclusion of injuries to the eyes of foresters and agricultural workmen. They consider it fair to reduce the compensation 10 to 20 per cent of the normal when there was a previous disease in the injured organ or when the patient opposed the performance of a surgical operation which might have restored the functional capacity of the organ.

They believe that the use of preventive devices to avoid accidents, such as goggles, spectacles and screens, should be made obligatory to workmen. They admit, however, that some of these devices are not practical or comfortable and should be improved.

After an exhaustive study of partial or permanent disabilities by several authors (Magnus, Groeunow and Truc) and in several countries, they propose a new table of incapacities, dividing them in three classes according to the visual requirements of different crafts, viz., those needing great visual acuity of vision, those with lower visual requirements and those calling for the use of only one eye. The indemnities which they advocate, and which they consider more practical in their country, are shown in tables.

MANUEL URIBE TRONCOSO.

Clinical Aspects of Ocular Involvement in Lepers. Monograph 4 of The Arquivos do Sanatorio "Padre Bento." By José Mendonça de Barros. Pp. 79, with 60 colored figures and 36 stereograms: Serviço de Profilaxia da Lepra, São Paulo, Brazil, 1939.

This excellent monograph deals with the ocular manifestations of leprosy in the anterior segment of the eye, especially as seen with the slit lamp microscope. The author has had the opportunity of examining about 1,200 lepers with ocular symptoms and has made beautiful colored illustrations and stereoscopic photographs of the changes found. These give the book the value of an atlas of ocular leprosy. He describes first the lesions in the skin and eyelids and then reports in minute detail the involvement of the conjunctivosclera in the form of nodular lesions, local and diffuse. He does not believe in the existence of isolated conjunctivitis in leprosy.

The corneal changes are studied first on the surface: epithelial edema, vesicles, erosions and band-shaped keratitis. In the corneal stroma appear conspicuously thickening of the nerves and nodular lesions in the form of rosary beads or fine infiltrations around the nerves. As a rule there is no development of blood vessels throughout the course of the infiltrations, except those observed in sclerosing keratitis and in severe iridocyclitis. On the endothelial surface there are bedewing, precipitates and opacities. Parenchymatous keratitis, including the punctate form, appears usually above the cornea, has a milky aspect and ends in complete sclerosis and blindness. The corneal lepromas are usually propagated from the sclera.

In the iris the involvement may occur as diffuse inflammation, acute or chronic, or as a localized miliary or nodular infiltration.

Thirty-six stereograms show well the gross corneal and iritic changes.

MANUEL URIBE TRONCOSO.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 33 Welbeck St., London, W., England.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen, Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. H. G. Ditroi, Szeged.
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, Maria ucca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the Secretary, Dr. Mohammed Khalil.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

OPHTHALMOLOGY SOCIETY OF BOMBAY

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

PALESTINE OPHTHALMOLOGICAL SOCIETY

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Dr. Malcolm Hepburn, 111 Harley St., London, W. 1, England.
Secretary: Dr. C. Dee Shapland, 15 Devonshire Pl., London, W. 1, England.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive.
All correspondence should be addressed to the President.

SOCIEDADE DE OPHTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Francisco Ferreira, Pitangueiras 15, Brotas, S. Salvador, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Albert C. Snell, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary: Dr. Derrick Vail, 441 Vine St., Cincinnati.
Place: Cleveland. Time: June 2-6, 1941.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Frank E. Brawley, 30 N. Michigan Ave., Chicago.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. F. P. Calhoun, 478 Peachtree St. N. E., Atlanta, Ga.
Secretary-Treasurer: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Place: Hot Springs, Va. Time: May 29-31, 1941.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. John Evans, 23 Schermerhorn St., Brooklyn.
Secretary-Treasurer: Dr. C. S. O'Brien, University Hospital, Iowa City.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. W. H. Lowry, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. Alexander E. MacDonald, 421 Medical Arts Bldg., Toronto.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President-Emeritus: Mr. William Fellowes Morgan, 50 W. 50th St., New York.
Secretary: Miss Regina E. Schneider, 50 W. 50th St., New York.
Executive Director: Mrs. Eleanor Brown Merrill, 50 W. 50th St., New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Charles W. Barkhorn, 223 Roseville Ave., Newark.
Secretary: Dr. William F. McKim, 317 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. V. May, 1703 Main St., Marinette.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.
Place: Wisconsin Rapids. Time: June 1941.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. William D. Rowland, 84 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. Trygve Gundersen, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Isaac H. Jones, 635 S. Westlake Ave., Los Angeles, Calif.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Clarence W. Shannon, 4th and Pike Bldg., Seattle.
Secretary-Treasurer: Dr. Purman Dorman, 1215–4th Ave., Seattle.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month, except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. W. E. Rideout, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. J. J. Potter, 303 N. Main St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. M. Kessler, 311 Center Ave., Bay City, Mich.
Secretary-Treasurer: Dr. J. H. Curts, 330 S. Washington Ave., Saginaw, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Davis, 1615 Howard St., Omaha.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux Falls, S. D.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Grady E. Clay, Medical Arts Bldg., Atlanta, Ga.
Secretary: Dr. John R. Hume, 921 Canal St., New Orleans.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. Franklin P. Maury, Professional Bldg., Tucson, Ariz.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. J. K. Heckert, 103 N. Washington St., Lansing.
Secretary-Treasurer: Dr. W. D. Irwin, 710 Hanselman Bldg., Kalamazoo.
Time: Third Thursday of alternate months.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. H. Bailey, 29 S. Oakland Ave., Sharon.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. R. R. Kirkpatrick, 6th and Walnut Sts., Texarkana, Ark.
Secretary-Treasurer: Dr. Raymond C. Cook, 701 Main St., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. William M. Bane, 1612 Tremont Pl., Denver.
Secretary: Dr. Harry Shankel, Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. W. E. McClellan, 750 Main St., Hartford.
Secretary-Treasurer: Dr. S. J. Silverberg, 201 Park St., New Haven.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. E. N. Maner, 247 Bull St., Savannah.
Secretary-Treasurer: Dr. C. K. McLaughlin, 567 Walnut St., Macon.
Place: Macon. Time: May 13-17, 1941.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S.E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Henry N. Blum, 912 American Bank Bldg., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. Erling Wilhelm Hansen, 78 S. 9th St., Minneapolis.
Secretary-Treasurer: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. Roy Grigg, Bozeman.
Secretary: Dr. A. W. Morse, 507 Phoenix Bldg., Butte.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. Edgar P. Cardwell, 47 Central Ave., Newark.
Secretary: Dr. Arthur E. Sherman, 243 S. Harrison St., East Orange.
Place: Atlantic City. Time: June 3-5, 1941.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Searle B. Marlow, 109 S. Warren St., Syracuse.
Secretary: Dr. C. Stewart Nash, 277 Alexander St., Rochester.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. M. R. Gibson, Professional Bldg., Raleigh.
Secretary: Dr. Vanderbilt F. Couch, 105 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. N. A. Youngs, 322 De Mers Ave., Grand Forks.
Secretary-Treasurer: Dr. F. L. Wicks, 516–6th St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Paul Bailey, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. R. S. Fixott, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. W. Carpenter, 200 E. North St., Greenville.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. J. W. Ward, 2607½ Lee St., Greenville.
Secretary: Dr. Dan Brannin, 929 Medical Arts Bldg., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. Rowland H. Merrill, 1010 First National Bank Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Earl H. Phillips, 628 Judge Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. George G. Hawkins, Newport News.
Secretary-Treasurer: Dr. Guy Fisher, 3 E. Beverley St., Staunton.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George E. Black, 7 W. Bowery St., Akron, Ohio.
Secretary-Treasurer: Dr. C. R. Andersen, 106 S. Main St., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Stacy C. Howell, 144 Ponce de Leon Ave. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., second Wednesday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Maurice Wieselthier, 1322 Union St., Brooklyn.
Secretary-Treasurer: Dr. Harold F. Schilback, 142 Joralemon St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. James G. Fowler, 412 Linwood Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Richard Gamble, 30 N. Michigan Ave., Chicago.
Secretary-Treasurer: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati Ophthalmic Club

Chairman: Each member, in rotation.
Secretary-Treasurer: Dr. E. R. Thomas, 819 Carew Tower, Cincinnati.
Place: Holmes Memorial Library, Cincinnati General Hospital. Time: 8:15 p. m., third Monday of each month except June, July and August.

Cleveland Ophthalmologic Club

Chairman: Dr. Albert D. Ruedemann, Cleveland Clinic, Cleveland.
Secretary: Dr. B. J. Wolpaw, 2323 Prospect Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Francis H. Adler, 313 S. 17th St., Philadelphia.
Clerk: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. C. D. Postle, 240 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Hugh C. Thompson, 289 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. F. K. Stroud, 416 Chaparral St., Corpus Christi, Texas.
Secretary: Dr. Arthur Padilla, 414 Medical Professional Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Dan Brannin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. L. E. Darrough, 4105 Live Oak St., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. L. A. Hulsebosch, 191 Glen St., Glen Falls.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. W. R. Thompson, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. A. E. Jackson, 602 W. 10th St., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Wallace W. Ralston, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. William J. Snow, 708 Medical Arts Bldg., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. M. Masters, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Homer Beal, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. Desmond Curran, Federal Reserve Bank Bldg., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Paul Southgate, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Kirt G. Parks, 605 Professional Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. John P. Lordan, 2007 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Colby Hall, 1136 W. 6th St., Los Angeles.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. E. J. Cummings, 1835 I St. N. W., Washington.
Secretary: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. John B. Hitz, 411 E. Mason St., Milwaukee.
Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Andrew Hollabaugh, Doctors Bldg., Nashville, Tenn.
Secretary: Dr. Guy Maness, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. Leonard C. Whiting, 121 Whitney Ave., New Haven, Conn.
Secretary: Dr. Frederick A. Wies, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Algernon Reese, 73 E. 71st St., New York.
Secretary: Dr. Brittain Payne, 35 E. 70th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President: Dr. Morris Davidson, 80 Centre St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. R. E. Leatherock, Cushing, Okla.
Secretary: Dr. Harry C. Ford, 1014 Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. Howard Heine, 635 N. Main St., Fremont, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President: Dr. L. Markowitz, 16 Church St., Paterson, N. J.
Secretary-Treasurer: Dr. A. John Reinhorn, 302 Broadway, Paterson, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Walter I. Lillie, 255 S. 17th St., Philadelphia.
Secretary: Dr. Edmund B. Spaeth, 1930 Chestnut St., Philadelphia.
Time: First Thursday of each month from October to May.

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward A. Weisser, 119–5th Ave., Pittsburgh.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. F. Bryce, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. Richard W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. E. J. Avery, 11 N. Goodman St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.
Place: Rochester Academy of Medicine, 1441 East Ave. Time: 5 p. m., Jan. 22. 1941.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. J. F. Hardesty, Missouri Theatre Bldg., St. Louis.
Secretary: Dr. Carl C. Beisbarth, 3720 Washington Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Dan Russell, 705 E. Houston St., San Antonio, Texas.
Secretary-Treasurer: Dr. P. G. Bowen, 315 Camden St., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Matthew Hosmer, 384 Post St., San Francisco.
Secretary: Dr. Fred Boyle, 490 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Louis A. Parsell, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. Robert L. Pohl, 407 Riverside Ave., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

SYRACUSE EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. R. Webster, State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. John R. Myers, State Tower Bldg., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. S. H. Patterson, 1251–15th St., Toledo, Ohio.
Secretary: Dr. J. E. Minns, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Frank Costenbader, 1726 I St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. L. Conner Moss, 1710 Rhode Island Ave. N.W., Washington, D. C.
Place: Episcopal Eye, Ear and Throat Hospital. Time: 7:30 p. m., first Monday in November, January, March and April.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.